ABSTRACTS OF WORLD MEDICINE

VOL. 8 No. 6 DECEMBER, 1950

Hygiene and Public Health

2200. **The Effectiveness of Vaccination Against Diphtheria.** (Sobre la eficacia de la vacunación antidiftérica) M. B. OTERO. *Acta Pediatrica Española* [*Acta pediatr. esp.*] **8**, 669–679, June, 1950. 4 figs., 15 refs.

In Spain 70% of the children who are immunized against diphtheria are under 5 years of age and 30% are between 5 and 15 years. There are 7,500,000 children under 15 years old and 2,810,000 have been immunized. In 80% of the children the antitoxin level in the blood amounted to $\frac{1}{10}$ unit, in 15% it varied between $\frac{1}{30}$ and $\frac{1}{10}$, and in 5% it was less than $\frac{1}{10}$. Immunization is now compulsory. The mortality from diphtheria has decreased from 25·1 per 100,000 in 1901 to 0·9 per 100,000 in 1948. Before the introduction of immunization against diphtheria the mortality rate in the years 1916 to 1936 decreased from 19·6 to 4·4 per 100,000 or in absolute figures from 4,000 to 1,100; in $6\frac{1}{2}$ years of immunization (1939 to 1946) it decreased from 15·6 to 0·9 per 100,000 or from 4,022 to 259.

Franz Heimann

2201. **Food Contamination from the New Insecticides** K. P. DUBOIS. *Journal of the American Dietetic Association* [*J. Amer. diet. Ass.*] **26**, 325–328, May, 1950. 9 refs.

Since 1942 two classes of chemical agents have been introduced as insecticides, the chlorinated hydrocarbons and related chlorinated compounds, and the organic phosphorus-containing compounds.

Chlorinated hydrocarbons rarely cause acute poisoning, but when sprayed on fruit they remain active for long periods and are potential sources of chronic poisoning. In addition, these fat-soluble compounds tend to be secreted in the milk of cows fed on treated pastures, and if contaminated milk or fruit be ingested the chlorinated hydrocarbons may become concentrated in the lipoid tissue, causing damage. Thus experimentally chronic intoxication has been produced in animals. So far the tolerance dose over long periods of ingestion has not been ascertained.

The organic phosphorus compounds in common use are hexaethyl tetraphosphate, tetraethyl pyrophosphate and "parathion" (*p*-nitrophenyldiethyl thionophosphate). These insecticides, particularly tetraethyl pyrophosphate, are highly toxic, and may give rise to acute poisoning by an inhibitory action on cholinesterase, producing stimulation of the central and peripheral nervous systems with possible death. Fortunately, these compounds are rapidly hydrolysed in contact with moisture, so that spray residues on plants are usually non-toxic before the food is consumed. No cases of chronic poisoning have been reported.

Among the organic phosphorus insecticides developed in Germany during the recent war is a systemic group. This type differs from others in being taken up by the plant from the soil. Before absorption by the plants, these systemic compounds are non-poisonous, but the plants convert them into toxic insecticidal substances, which theoretically may give rise to poisoning in man. However, it is found that as the plants mature the toxicity of the systemic compounds lessens, so that by the time the plants are ripe they are harmless. Experiments are now in hand to determine the effects of acute and chronic poisoning caused by the ingestion of unripe plants contaminated with one of these compounds (octamethyl pyrophosphoramide: "OMPA": "pestox III"). Until the toxic effects of these systemic insecticides are determined, these products should be employed with great caution. *A. Michael Critchley*

2202. **Aircraft Desinsectisation in West Africa** L. J. BRUCE-CHWATT and KEE HOCK OOI. *Monthly Bulletin of the Ministry of Health, etc.* [*Mon. Bull. Min. Hlth*] **9**, 142–147, June, 1950. 2 refs.

The tests described in this paper were made at the Lagos Airport in Nigeria during the height of the dry season. Experimental spraying was carried out in two types of aircraft: the "Dove" used for local communications and having a capacity of 400 cubic feet (11·3 c.m.) and the "Wayfarer" used mostly for inter-colonial communications and having a capacity of 1,700 cubic feet (48 c.m.). The test insects were *Aëdes aegypti* and *Anopheles gambiae*, cages containing the mosquitoes being placed in three situations in the machines—the cockpit, the cabin, and the tail. Two types of aerosol dispensers filled with insecticide were tested, a CO_2-propelled dispenser and a low-pressure "freon"-propelled dispenser.

The results obtained under these conditions suggest that: (1) *A. gambiae* is more sensitive to the agents tested than is *A. aegypti*; (2) a smaller proportion of the mosquitoes occupying the tail of an aeroplane is killed than is the case in the cabin or in the cockpit; (3) the temperature at 10 a.m. in the passenger cabin of a "Dove" recently landed at Lagos was found to be 97 to 105° F. (36 to 40·6° C.) and the humidity 60%. Such conditions could hardly be inflicted on passengers for any prolonged period, and the authors therefore recommend that the usually advocated 5- to 10-minute

exposure time after spraying should be reduced to a maximum of 3 minutes; they consider, however, that this shortening of the period should be coupled with an increase in dosage amounting to at least 15 g. of a standard insecticide aerosol per 1,000 cubic feet (28·3 c.m.); (4) the low-pressure freon-propelled dispenser filled with ·3% pyrethrin formulation compared favourably with the CO_2 dispenser filled with the insecticide " R. 587 ", containing approximately 0·4% pyrethrins; (5) in order to produce an adequate kill a dosage of at least 0·06 g. pyrethrins per 1,000 cubic feet should be employed. *R. M. Gordon*

2203. **Salmonellosis**
J. GRANT. *Medical Officer* [*Med. Offr*] **84**, 5–9 and 19–22, July 1 and 8, 1950. 20 refs.

In the first part of this article the author describes his experience of salmonellosis in a county borough from 1936–49 with reference to the prevalence, aetiology, and epidemiology of the infection, the discovery and disposal of patients, the clinical course of the illness and its treatment, and the problem of the carrier condition. In the second part he discusses the more general aspects of salmonellosis, with sections on diagnosis and treatment, mammalian and avian infections, and measures for suppression. The author regards salmonellosis as an infectious disease with case-to-case and carrier-to-case transmission in addition to typical food-poisoning outbreaks. In support of his view he quotes statistical, clinical, and epidemiological findings.

Excluding the enteric fevers, 77 cases of illness due to infection with salmonellae (with 4 deaths) were discovered during 1936–49, in the area concerned, 37 of them occurring in seven outbreaks of food-poisoning and 40 among patients admitted to hospital for various acute conditions. The recent history was investigated and faeces examined of members of infected households and, later, supervision of convalescents and carriers was undertaken. *Salmonella typhi-murium* accounted for 58 cases (4 deaths), *S. thomson* for 13, *S. stanley* for 3, *S. montevideo* for 2, and *S. anatum* for 1. Among the 77 patients there were 12 who were infected by a previous case in the household, 2 by household carriers, and one to whom the infection passed from a patient via two known carriers. Of 50 patients and 16 carriers, more than half ceased to excrete the organisms within one month, but 11% carried them for over 3 months.

The need for speedier bacteriological diagnosis is discussed, as also is the value of chloramphenicol in the treatment of cases and carriers. The author points out that the accepted view of salmonellosis, based on the work of Savage and White and recently re-expressed in a Ministry of Health Memorandum on Food Poisoning (1949) is not in accord with his recent experiences, in that transmission of the infection from case to case and its spread by human carriers are generally thought to occur rarely, if at all. In his view, salmonellosis has emerged in the last 3 years as a specific alimentary infection, increasing in virulence and spreading by infective convalescents and carriers, outbreaks of food poisoning being " but the most dramatic high lights of what is an essentially infectious disease ". The author believes that salmonellosis will become endemic in Great Britain unless adequate suppressive measures are taken among both human beings and animals. *Joyce Wright*

2204. **The Control of Culicine Mosquito Breeding in Septic Tanks by Means of D.D.T. Bricks**
C. E. SHEARMAN. *Journal of the Royal Army Medical Corps* [*J. R. Army med. Cps*] **94**, 259–265, May, 1950. 1 fig.

2205. **Dental Structure and Caries in 5-year-old Children Attending London County Council Schools. Results of Five Surveys (1929–49)**
H. MELLANBY and M. MELLANBY. *British Medical Journal* [*Brit. med. J.*] **1**, 1341–1343, June 10, 1950. 10 refs.

EPIDEMIOLOGY

2206. **Food-poisoning in Sheffield in 1949**
E. L. M. MILLAR and M. POWNALL. *British Medical Journal* [*Brit. med. J.*] **2**, 551–553, Sept. 2, 1950.

The authors describe four trivial outbreaks of food poisoning due to *Staphylococcus aureus* toxin. In one of these outbreaks a staphylococcus of a bacteriophage type frequently associated with food poisoning was traced in the food and in the victim. One of the 2 men who made the galantine suspected as the vehicle of poisoning had a mild dermatitis of the hands and wrists. Staphylococci of the food-poisoning type were recovered from his hands but not from his nose. In another outbreak cooked tongue was the vehicle, and staphylococci of the food-poisoning type were recovered from three members of the butcher's family.

The authors complain that, although food poisoning is made notifiable by the Food and Drugs Act, 1938, the great importance of immediate notification seems not to be generally realized. Without this, prompt investigation is impossible. *W. H. Bradley*

2207. **Epidemiologic Aspects of Hepatitis in U.S. Troops in Germany 1946–1950**
J. R. PAUL and H. T. GARDNER. *American Journal of Medicine* [*Amer. J. Med.*] **8**, 565–580, May, 1950. 14 figs., 34 refs.

The incidence of infective hepatitis among American occupation forces in Germany from 1946 to 1950 continued to be high. A peak was reached in the autumn and winter of 1949 but the seasonal curve among the troops consistently showed deviations from the usual rise in autumn and the early winter decline noted among civilian populations, a primary peak occurring in September to November and a secondary one during February to March. This suggests that in addition to cases of true infective hepatitis some cases of hepatitis were transmitted by infected syringes and needles. Among British troops stationed in Germany during the same period there was only the primary autumnal rise.
G. M. Findlay

2208. **The Distribution of Incubation Periods of Infectious Disease**

P. E. SARTWELL. *American Journal of Hygiene* [*Amer. J. Hyg.*] **51**, 310–318, May, 1950. 2 figs., 21 refs.

The epidemic curve and frequency distribution of incubation periods in outbreaks of bacterial food poisoning, streptococcal sore throat, salmonellosis, bacillary dysentery, poliomyelitis, measles, typhoid fever, chickenpox, amoebic dysentery, serum hepatitis, common cold (experimental), induced malaria, and poliomyelitis (experimental in the monkey) as reported in the literature have been studied. When the frequency distribution of incubation periods was plotted on normal probability paper, cumulative percentages against the logarithm of the period of incubation, a normal, linear plot was usually obtained. The mean length of the incubation period apparently does not affect the degree of variation, since both in diseases with very short and in those with very long incubation periods the distribution conformed to a normal pattern.

From the frequency curves thus plotted for 18 published sets of observations the author calculated an estimated median value and a " dispersion factor " in each case, the logarithm of the estimated median value being taken as the point where the curve intercepted the 50% frequency. The dispersion factor was the antilogarithm of the standard deviation of the distribution, as read (in logarithms) from the curve. For the diseases studied the estimated median incubation period varied from 2·3 hours for bacterial food poisoning to 105 days for serum hepatitis. The dispersion factor for 17 of the 18 outbreaks studied varied only from 1·14 to 1·58, the exception being amoebic dysentery with a value of 2·11. The median incubation values estimated by this method from three separate sets of data for measles were in good agreement, as were those from 2 sets of data for chickenpox. There was a difference of 4·4 days between the estimated median values of the incubation periods of 2 food-borne typhoid outbreaks, and 5 days between those of two epidemics of serum hepatitis. *W. J. Martin*

2209. **A Survey of the Epidemiology of Diphtheria in North-west Europe and North America in the Period 1920–1946**

J. W. MCLEOD. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 137–156, April, 1950. 12 figs., bibliography.

The contrasts in diphtheria incidence in different countries during the last 10 years are remarkable. The author discusses factors which may have contributed to these variations. The factors include the ratio of rural to urban population, the effect of natural immunization of a community by epidemic diphtheria, the influence of dietetic deficiency and of migrations of population, and the effect of prophylactic inoculation and of the strain of *Corynebacterium diphtheriae* causing an epidemic. The argument is illustrated by charts of the case incidence in several countries and cities. These charts provide certain interesting contrasts and resemblances. For example, in Norway, Holland, and Denmark a high or relatively high incidence of diphtheria in the years immediately after the 1914–18 war was followed by a decline, until in the years immediately preceding the 1939–45 war the incidence had become almost negligible. This low incidence of diphtheria was independent of inoculation of the population; the decline in incidence in Norway and Denmark occurred when the extent of mass inoculation was far below the 60 to 70% level to which a similar low diphtheria incidence in Canada and U.S.A. has been attributed. It may, however, be significant that in the three European countries mentioned diphtheria incidence rose during the 1939–45 war while no similar rise occurred in North America. In England and Scotland there was a remarkable decline in 1939–45 after the incidence had been maintained at a moderately high level from 1920. The decline occurred at a time when there was marked epidemic incidence in Western Europe.

Although bacteriological information is restricted, the data presented establish clearly enough the importance of the role of *C. diphtheriae* gravis in epidemic diphtheria. The question whether the gravis strain appears as a mutation or whether it acts independently of the other types in producing waves with high epidemic potential is discussed, but no conclusion reached.

As regards the influence of mass inoculation, it is clear that prophylactic inoculation of less than 60 to 70% of the total child population, a level considered to be essential to get the full effect of this measure, will not prevent the occurrence of very sharp epidemics of diphtheria. Examples of failure in Leeds, Halifax (Nova Scotia), and Amsterdam are given. The charts also show the importance of taking account of the immunizing effect of a severe diphtheria epidemic on a community, and of not attributing to prophylactic inoculation alone results which are most probably due to the combined effect of that procedure and other factors, such as those presumably accounting for the negligible incidence of diphtheria in Holland and Norway in the years 1935 to 1940. That gravis diphtheria might, at any time, break through a high level of immunity in a herd is clear, but the great value of inoculation in almost completely eliminating fatal cases cannot be over-emphasized.

W. H. Bradley

2210. **Clinical Observations in an Epidemic of Harvest Fever.** (Klinische Beobachtungen bei einer Feldfieber-epidemie)

S. LITZNER and H. HAHN. *Deutsche Medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **75**, 882–886, June 30, 1950. 1 fig.

Harvest fever, caused by one of three species of leptospira, *L. grippo-typhosa*, *L. sejroe*, and *L. australis*, is unknown in Great Britain. It is rare in western Germany, and the author of this interesting paper describes in detail the clinical features of the disease as observed in 1949 during the first epidemic to be recorded in Lower Saxony, in the district of Wolfenbüttel. In July and August 43 patients were admitted to the municipal hospital there, most of whom had been engaged in the harvesting of peas, while in the few remaining cases contact with freshly harvested peas, or in one case with the fields from which these had been

harvested, could be proved. Headache and pains in the limbs and joints were typical initial symptoms, and giddiness, nausea, and vomiting were also common. The temperature was 39° to 40° C. (102·2° to 104° F.), and usually fell by lysis over a period lasting up to 14 days; after an afebrile interval of 1 to 5 days a secondary rise was frequently observed for 1 to 4 days. Injection of the conjunctiva and sclera was common. Jaundice was not observed, but rashes of varying description and intensity were frequent. Complete recovery took 10 to 12 weeks, or even longer; no fatalities were reported. The incubation period was 9 to 16 days. Positive agglutination reactions were obtained in all cases, and leptospirae were also cultured from the blood. Coincidentally with the occurrence of this epidemic a large increase of the murine population was noticed, and leptospirae were isolated from the kidneys of over 80% of mice trapped in the area.

W. G. Harding

INDUSTRIAL MEDICINE

2211. **Studies on Aerosols. IX. Enhancement of Irritating Effects of Various Substances on the Eye, Nose, and Throat by Particulate Matter and Liquid Aerosols in Connection with Pollution of the Atmosphere.** [In English]

L. DAUTREBANDE and R. CAPPS. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **82**, 505–528, 1950. 8 figs., 31 refs.

In relation to the eye, nose, and throat irritation caused by the Los Angeles " smog ", several experiments have been performed. Although the maximal concentration of SO_2 found in the Los Angeles atmosphere is far less than that producing irritation of the ocular mucosa, it is known that the atmosphere contains a large number of other materials (dust, oil fumes, and sodium chloride in aerosol form) apart from the more obviously toxic organic and other compounds. It appeared possible that the limitation of irritation to the eye, nose, and throat might be due either to the slow build-up of an irritant concentration by surface adsorption or to agglomeration of the particles to such a size (5 to 10 μ) as to prevent penetration to the lungs. Accordingly, 84 subjects were exposed for periods of 10 minutes to various concentrations of known eye irritants, with or without the addition of particulate matter (carbon black) or aerosols of motor oil or sodium chloride. Such additions increased the irritant effect of SO_2 and SO_3.

Low concentrations of SO_2 and SO_3 not causing irritation of the eye after 10 minutes did cause definite irritation of eye, nose, and throat when particulate matter or oil or sodium chloride aerosols were also present. Atmospheres containing 0·2 to 0·3 p.p.m. of carbon black (containing 10% of diesel oil) or aerosols of used motor oil (1·3 to 2 p.p.m.) were by themselves irritant. On the other hand, fresh mineral oil aerosols even up to 300 p.p.m. had no irritant effect. It is considered that the eye, nose, and throat irritation during smog days is more closely related to the presence of particulate matter than to the irritant gases and vapours known to be present. The temperature conditions on such days are such as to increase at ground level the concentration of particulate matter discharged into the air. Water sprays effectively remove from the atmosphere particles greater than 1 to 2 μ in size. A decrease in temperature and an increased relative humidity bring about the formation of large droplets and aggregates in sodium chloride aerosols, and this may be an important factor in the production of large particles in atmospheres near the sea. It is believed that if the amount of particulate matter in the Los Angeles atmosphere could be reduced during smog days, then the vapours and gases present would not themselves be irritant. *Derek R. Wood*

2212. **The Industrial Employee with Myocardial Infarction. His Ability to Return to Work**

R. B. CRAIN, M. E. MISSAL, and K. W. WILSON. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **1**, 525–538, May, 1950. 14 refs.

A series of 184 cases of myocardial infarction occurring among 30,000 employees during a 20-year period ending December, 1948, has been analysed. After the first infarction 8% died immediately, but of the remainder 86% returned to work. The period of convalescence varied from 2 to 6 months and care was taken to rehabilitate the patient, when necessary, either by giving temporary part-time employment or by changing the nature of his work. Of the total number 72% were alive at the end of 1948, and 51%—or 71% of those living—were still working. The presence of concomitant hypertension affected adversely the chance of a man's returning to work and his expectation of life. None with hypertension lived more than 8 years, while 5 without it were alive more than 10 years later.

C. W. C. Bain

2213. **Dermatological Hazards in the Cigar Industry**

M. H. SAMITZ, P. MORI, and C. F. LONG. *Industrial Medicine* [*Industr. Med.*] **18**, 434–439, Oct., 1949. 5 refs.

An investigation of the dermatological hazards in the cigar industry was carried out at one very large and two smaller manufacturing plants in the U.S.A. The cigar manufacturing processes, described in considerable detail, call for strict control of temperature and humidity. Mechanization has changed the industry, the various processes being now carried out exclusively by women. The agents responsible for skin affections are tobacco, friction and moisture, machinery (trauma), and dust and vapours. In 1940 in the large plant, eruptions began to appear on the hands of the girls who applied the wrapper layer of leaf and of the examiners. These workers apply gum tragacanth paste with the fingers to minor defects in the cigar. Tobacco sensitivity, observed only infrequently in the industry, and sensitization to other substances, including the paste, were eliminated by patch testing. Observation of the examiners at work suggested that the skin eruptions were caused by the wetness of their hands and the alkaline reaction of the towelling constantly in use. Determinations of the *p*H of the hands of the affected employees, their towelling, and the paste,

indicated abnormal alkalinity of all three. In contrast to these findings, no case of hand eruption occurred in the smaller plants where boric acid was incorporated in the paste and where paper towels were used and then discarded.

The authors concluded that the alkaline medium, together with constant exposure to moisture, lessened the alkali-neutralizing capacity of the skin and this, " with the keratin solvent and degreasing action of the alkalies, favored the formation of the dermatitis ". It was more common in the winter, and it was suggested that exposure to the winter air outside the working environment may have been the exciting factor. In 9 years 1,065 cases were seen, the majority being mild and only rarely necessitating absence from work; during one year the hand eruptions were the cause of only 0·04% of all visits to the works surgery. *A. J. Amor*

2214. **Incidence of Cancer in the Carbon Black Industry**
T. H. INGALLS. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **1**, 662–676, June, 1950. 4 figs., 16 refs.

A study was made to determine whether an industrial hazard of cancer does or does not exist in the manufacture of carbon black, a commercially produced form of soot. In a company employing on the average 476 carbon black workers annually, 1 man died of cancer of the stomach during a 10-year period, 1939 to 1949, and cancer of the skin developed in 2 other employees during a 5-year period, 1944 to 1949. The observed death rate from cancer among carbon black workers, 0·21 per thousand per work year, is low as judged by the rates observed among other comparable groups of the industrial and general population. The morbidity rate of 1·0 new case annually per thousand workers per work year is likewise low and no higher than expectancy. The available clinical and epidemiologic evidence indicates that the carbon black worker faces no more than the ordinary risks of cancer encountered by other groups of the male working population.—[Author's summary.]

2215. **Stannic Oxide Pneumoconiosis**
C. C. DUNDON and J. P. HUGHES. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **63**, 797–812, June, 1950. 10 figs., 21 refs.

Three reports describing the occurrence of a benign pneumoconiosis in workers exposed to stannic oxide, chiefly in the calcining of scrap tin, are quoted; a further case in a man who had worked a detinning furnace for 18 years and died of carcinoma of the prostate is added. The patient had no symptoms of respiratory disease. Radiography showed uniform, discrete, intensely opaque nodulation over both lung fields.

The necropsy findings were complicated by the presence of neoplastic metastases and bronchopneumonia. There were, however, focal deposits of dark-brown or black pigment, corresponding to the radiological opacities; their distribution was typical of dust deposition, for they were found in the alveolar walls, lymph vessels, and lymphatic aggregates. Connective tissue round pigment-choked lymphatics showed some loose collagen fibres " without hyalinization ". The lymph nodes contained much pigment but their structure was normal. Chemical analysis of sections of lung after micro-incineration gave positive results for tin. Spectrographic analysis showed that the ratio of stannic oxide to ash in the material was 13·4%; silica content was normal. *X*-ray diffraction analysis confirmed the above.

It is suggested that stannic oxide in furnace-fume is more likely to cause the condition than is dust from the industrial handling of stannic oxide. *L. W. Hale*

2216. **Injuries of the Semilunar Cartilages in Miners: A Review of 200 Cases, with Special Reference to the Post-operative Disability Time**
A. A. BONAR. *Glasgow Medical Journal* [*Glas. med. J.*] **31**, 197–205, June, 1950. 5 refs.

A series of 200 cases of meniscectomy performed on miners is reviewed. Re-calculation of data given in the paper shows that the relation of observed to expected injuries to semilunar cartilages expressed as a percentage is 172 in coal-face workers, 69 in workers employed on roads, 50 in putters, 90 in safety men, firemen, and chargemen, and 32 in craftsmen. Of the whole group, 94% returned to their pre-accident work and 6% (11) were unfit to resume their pre-accident work. Injuries are more common in young adults (though this may be because they are doing the heaviest work). The average period of disability was just over 80 days after medial and lateral meniscectomy and nearly 200 days after bilateral meniscectomy. Young miners made the quickest recovery. The period of disability is not affected by the nature of the individual miner's work. While minor degrees of arthritic change do not seriously affect operative results, results of meniscectomy in joints affected by severe arthritis are discouraging. Osteo-arthritis or associated ligamentous injury causes permanent partial disablement. *T. A. Lloyd Davies*

2217. **Further Observations on the Pathological Physiology of Chronic Pulmonary Granulomatosis Associated with Beryllium Workers**
R. A. BRUCE, F. W. LOVEJOY, P. N. G. YU, R. PEARSON, and M. MCDOWELL. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 29–44, July, 1950. 6 figs. 9 refs.

Three more cases of chronic pulmonary granulomatosis associated with beryllium compounds have been studied with reference to pulmonary and circulatory functional capacity. Despite obvious variations in clinical patterns of disease between patients, certain nonspecific general trends of functional disturbance appear common to most of these patients. They are restricted complemental air volume, increased mid-capacity-arterial oxygen gradient, hypoxemia, and hyperventilation on exertion. The complexity of factors contributing to the widened oxygen gradient is discussed. A general quantitative estimate of disability in relation to moderate exercise is expressed in terms of the physical fitness index. Untoward responses to continuous oxygen therapy are recorded.—[Authors' summary.]

Physiology and Biochemistry

2218. **Maternal Nutrition and Hydrocephalus in Newborn Rats**

A. G. HOGAN, B. L. O'DELL, and J. R. WHITLEY. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 293–296, June, 1950. 3 refs.

In previous experiments on rats consuming a synthetic diet a certain number of the young developed hydrocephalus; when folic acid was added to the diet the incidence of hydrocephalus was sharply reduced. This observation suggested a nutritional cause of the abnormality.

In the present series female rats were given a synthetic diet in which the protein was supplied by soy-bean oil meal together with a vitamin mixture including all recognized vitamins with the exception of ascorbic acid, nicotinic acid, folic acid, and vitamin B_{12}. The incidence of hydrocephalus in the offspring was less than 1%. In order to reduce the amount of folic acid available, a folic acid antagonist (methylfolic acid) was added to the same diet; the incidence of hydrocephalus then rose to over 20%. The type of diet used during the pre-experimental period determined the time that elapsed before hydrocephalus appeared in the offspring during the experimental period and had also a considerable influence on the incidence of hydrocephalus.

The authors confirmed the observations of Gillman *et al.* (*S. Afr. J. med. Sci.*, 1948, **13**, 47) that injection of trypan blue into female rats causes hydrocephalus in about 7·3% of the offspring. They think that the initial damage leading to hydrocephalus may be the same whether trypan blue or methylfolic acid is administered to the female rats.

[This is another important paper showing that the frequency of a congenital malformation may be enhanced by a specific deficiency in the diet during pregnancy.]

Z. A. Leitner

2219. **The Second Pancreatic Hormone affecting Carbohydrate Metabolism (Glucagon) and its Origin in the α-Cell System.** (Über das zweite Kohlenhydratstoffwechselhormon der Bauchspeicheldrüse (Glucagon) und seine Herkunft aus dem α-Zellensystem)

K. GAEDE, H. FERNER, and H. KASTRUP. *Klinische Wochenschrift* [*Klin. Wschr.*] **28**, 388–393, June 15, 1950. 8 figs., 27 refs.

A brief review is given of the evidence that the pancreas contains a factor which has an effect on carbohydrate metabolism opposite to that of insulin. This substance may be present in many preparations of insulin as an impurity, because it is precipitated by picric acid, trichloroacetic acid, and 75% alcohol. But, unlike insulin, it is only partly precipitated by salt; by salting out a solution of insulin, a liquor may be obtained which raises the blood sugar level when given intravenously and has only a minor degree of hypoglycaemic activity; it has more effect on well-nourished than on starved animals (dogs). This hypothetical factor, named "glucagon", is obtainable from horse, sheep, and pig pancreas.

In an attempt to determine the site of origin of glucagon, experiments were conducted in which this hyperglycaemic substance was obtained from the pancreas of dogs made diabetic by administration of alloxan, the pancreatic tissue therefore having a much reduced content of beta-cells. In a further experiment on a dog, the pancreatic duct was tied off, thus causing atrophy of all the external secretory cells of the gland. Two to 3 months later the dog was given a dose of alloxan which would normally be certain to cause diabetes mellitus owing to atrophy of the beta-cells; but in this case hyperglycaemia and glycosuria did not set in. This was in accordance with the findings of other workers, who have given alloxan to dogs in which the pancreatic duct had previously been tied, and was attributed to fatty degeneration of the liver, which was present in an advanced stage. On section, the dog's pancreas was found to be composed mainly of fibrous tissue, with scanty and atrophied islets consisting almost entirely of alpha-cells. An extract of this pancreas when injected into another dog had a hyperglycaemic action only; this was not very strong, presumably owing to the atrophy of the alpha-cells from which the hyperglycaemic factor must have been derived.

The authors therefore suggest that the chain of evidence is thus complete, and that the alpha-cells of the pancreatic islets secrete a substance (glucagon) which has a hyperglycaemic action; it is probably this which is responsible for the initial rise in blood sugar level which follows the intravenous injection of many preparations of insulin.

H. K. Goadby

2220. **The Carotid Sinuses and Cardiac Output.** (Sinus carotidiens et débit cardiaque)

G. R. DE VLEESCHHOUWER, R. PANNIER, and A. L. DELAUNOIS. *Archives Internationales de Pharmacodynamic et de Thérapie* [*Arch. int. Pharmacodyn.*] **83**, 149–157, 1950. 2 figs., 8 refs.

Because conflicting reports had been published on the effect on cardiac output of changes in carotid sinus pressure, some further experiments were performed in the Heymans Institute at the University of Ghent.

Cardiac output was determined in anaesthetized dogs by the direct Fick method, samples of mixed venous blood being obtained by catheterization of the right ventricle through the external jugular vein. Oxygen consumption was continuously recorded. In intact animals, bilateral carotid occlusion caused a hypertension accompanied by an increase in cardiac output in 7 dogs and by a fall in 3 dogs. The average rise in blood pressure was 30% and the average increase in cardiac output 59·7%. In vagotomized animals there was a

greater increase in blood pressure (average, 64·7%), cardiac output increasing by an average of 38·7% (increased in 8, decreased in 2 dogs). No correlation was observed between increase in blood pressure and increase in cardiac output. Further, the reflex hypertension was greater in vagotomized than in normal animals, while the cardiac output increase was greater in the normal dogs. *Derek R. Wood*

2221. **Effects of Heat and Cold on the Distribution of Blood within the Human Body. Radiological Investigations of the Liver, Lungs and Heart**
E. M. GLASER, F. R. BERRIDGE, and K. M. PRIOR. *Clinical Science* [*Clin. Sci.*] **9**, 181–187, May 30, 1950. 2 figs., 15 refs.

The authors report their observations on radiographs of the liver, lungs, and heart taken on 7 normal subjects in standard cold and warm environments. They found that, radiologically, the contour of the liver was larger and the pulmonary vascular shadows were wider and more numerous when the skin was cooled than when it was warmed. No significant variations were noted in the transverse diameter of the heart. These findings suggest that changes in the outside temperature cause a redistribution of blood between the superficial skin vessels and the inside organs of the body according to the need to preserve or dissipate heat. *S. Karani*

2222. **Antagonism of Adrenocorticotrophic Hormone and Adrenal Cortical Extract to Desoxycorticosterone: Electrolytes and Electroshock Threshold**
D. M. WOODBURY, CHI-PING CHENG, G. SAYERS, and L. S. GOODMAN. *American Journal of Physiology* [*Amer. J. Physiol.*] **160**, 217–227, Feb., 1950. 3 figs., 19 refs.

Rats treated by the subcutaneous implantation of deoxycortone acetate (DCA) showed an increase in plasma sodium and a decrease in plasma potassium, chloride, and magnesium content, the plasma calcium level remaining constant. Concomitantly with these changes there was an increase in the threshold of the nervous system to the induction of convulsions by electric shock. Administration of either adrenocorticotrophic hormone (ACTH) or adrenal cortical extract (A.C.E.) to DCA-treated animals restored both the plasma sodium level and the electric-shock threshold to normal, but only partially restored the plasma chloride value and did not significantly affect the potassium level. ACTH also restored the plasma magnesium content to normal levels. The adrenals of DCA-treated rats weighed less than those of normal controls, probably owing to inhibition by the DCA of pituitary adrenocorticotrophic activity. The administration of ACTH produced adrenal hypertrophy in rats which had not received DCA, and partially restored the adrenal weight in DCA-treated rats. ACTH failed to lower the raised electric-shock threshold of rats treated with DCA after adrenalectomy.

There is thus experimental evidence to suggest that ACTH and A.C.E. may be able to correct either an excess or a deficiency of sodium in the plasma, whereas DCA acts only to increase the plasma sodium level. It is also suggested that some of the toxic effects of DCA described by Selye (*J. clin. Endocrinol.*, 1946, **6**, 117) may be due to inhibition of pituitary adrenocorticotrophic activity, thus producing a deficiency of adrenal cortical secretion. *G. Ansell*

RESPIRATORY SYSTEM

2223. **Ventilatory Function Tests. I. Voluntary Ventilation Capacity**
J. S. GRAY, D. R. BARNUM, H. W. MATHESON, and S. N. SPIES. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 677–681, June, 1950. 13 refs.

The aim of this work, undertaken at the Northwestern University Medical School, Chicago, was to find a reliable method for the determination of the so-called voluntary ventilation capacity, that is, the capacity when the subject breathes voluntarily at the maximum rate. The results of the tests were expressed in litres per minute. The procedure was standardized in such a way as to eliminate many factors, such as acapnia, involuntary inhibition of respiration, and individual differences in performance of breathing, which made the results of previous investigators unreliable.

In 283 healthy young men and 40 healthy young women the normal values were 167 ± 21 and 116 ± 21 litres a minute respectively, with reliability coefficients of 0·8 to 0·9. *A. I. Suchett-Kaye*

2224. **Ventilatory Function Tests. II. Factors Affecting the Voluntary Ventilation Capacity**
H. W. MATHESON, S. N. SPIES, J. S. GRAY, and D. R. BARNUM. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 682–687, June, 1950. 2 figs., 5 refs.

An experimental investigation in healthy young adults was designed to find out to what degree the following 3 factors affect the voluntary ventilation capacity. (1) *Vital capacity* in 194 healthy male subjects averaged $5·13 \pm 0·66$ litres and in 40 healthy female subjects $3·58 \pm 0·53$ litres; the voluntary ventilation capacity was found to correlate weakly (0·4 to 0·7) with the vital capacity, and the capacity ratio obtained by dividing the ventilation capacity by the vital capacity (and expressing the ventilation capacity in terms of each litre of vital capacity) remained constant when the other factors (muscular force and pulmonary resistance) remained unchanged. Abnormalities in the capacity ratio therefore indicated deviation from normal as regards either muscular force or air-flow resistance. The mean value of the capacity ratio was found to be 32·8 (for both men and women). (2) *Maximum expiratory pressure* was found to be 140·8 mm. Hg in 54 healthy individuals blowing through a mouth-piece into an aneroid manometer. No correlation could be established between the ventilation capacity and the maximum expiratory pressure in the normal people investigated. The results indicated that the effects of the latter would be small unless there was gross muscular impairment. (3) *Air-flow obstruction.* The introduction of artificial

air-flow resistances profoundly depressed the voluntary ventilation capacity and the capacity ratio, without altering vital capacity.

It is concluded that the estimation of the voluntary ventilation capacity is a more accurate measure of the pulmonary function than the much-abused vital capacity test, by which only one of the factors influencing the ventilation capacity is assessed. *A. I. Suchett-Kaye*

2225. **Ventilatory Function Tests. III. Resting Ventilation, Metabolism, and Derived Measures**
H. W. Matheson and J. S. Gray. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 688–692, June, 1950. 11 refs.

This paper is concerned with the results of various procedures for testing ventilatory function in 100 young healthy adult subjects. A critical evaluation is given of the performance and reliability of such tests as the measurements of voluntary ventilation capacity, vital capacity, resting pulmonary ventilation, and resting oxygen consumption, and of the three derived measurements of resting ventilatory reserve, capacity ratio, and ventilation equivalent for oxygen. Based on the above considerations, the authors present a scheme for the classification of impairment of pulmonary ventilatory function under two main headings: (1) reduction in resting ventilatory reserve; (2) excessive pulmonary ventilation. *A. I. Suchett-Kaye*

2226. **Respiration without Chemoreceptors.** (Die Atmung ohne Chemoreceptoren)
H. Winterstein. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **83**. 80–90, 1950. 2 figs., 10 refs.

Bilateral section of the vago-sympathetic trunk and removal of the carotid sinus areas gives a preparation without chemoreceptors, allowing observations to be made of the direct actions on the respiratory centre of changes in CO_2 tension and hydrogen concentration (*c*H) in blood. When acid is injected intravenously, CO_2 tension is reduced and *c*H increases in the blood. Respiration in such a preparation is stimulated. Anoxia due to deficiency of oxygen in the inspired air causes a fall in respiration, the CO_2 tension usually increasing and the blood *c*H falling. This evidence indicates that it is the *c*H rather than the CO_2 tension in the blood which is concerned in the direct regulation of respiration. In animals without chemoreceptors, asphyxial convulsions often do not occur after haemorrhage or clamping of the cerebral arteries. *Derek R. Wood*

NERVOUS SYSTEM

2227. **The Vomiting Center. A Critical Experimental Analysis**
S. C. Wang and H. L. Borison. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **63**, 928–941, June, 1950. 6 figs., 19 refs.

The authors, working at Columbia University, attempted to locate the vomiting centre by stimulation and ablation experiments. After failure of attempts to induce emesis electrically in cats under thiopentone anaesthesia, they explored with the Horsley–Clarke stereotaxic instrument the medulla of 20 decerebrate cats and found, as they have previously reported (*J. Neurophysiol.*, 1949, **12**, 305), that the only area of the brain-stem whose electrical stimulation caused vomiting was the dorso-lateral portion of the reticular formation, including the tractus solitarius and its nucleus.

The ablation experiments were performed on dogs since these animals, unlike cats, have fairly constant vomiting thresholds to apomorphine by injection and to copper sulphate by mouth, both of which can be determined experimentally. Two groups of chronic ablation experiments were performed. In the first, a superficial area of the floor of the fourth ventricle limited to the dorsal vagal nuclei was destroyed with the cold cautery; in the second, deep bilateral lesions were made with the loop electrode in the dorso-lateral portion of the reticular formation, corresponding to the area whose stimulation caused vomiting. The proximity of the lesions in this second group to the vital centres made it difficult to keep these preparations alive and, in those which survived, the complete destruction of the vomiting centre could not be assumed; therefore, the pre-operative and post-operative vomiting thresholds were compared. The 8 dogs with superficial lesions became refractory to apomorphine but the threshold to copper sulphate was only slightly increased. The 5 dogs surviving the deep medullary lesions in suitable condition for tests became refractory to apomorphine, and the threshold to copper sulphate was raised six-fold to eight-fold. The extent of the lesions was confirmed in both groups histologically.

From both series of experiments it is concluded that the vomiting centre lies deep in the medulla and that the dorsal vagal nucleus is only an afferent station on which the central emetic, apomorphine, acts. The authors rightly point out that the responsive region is not a single " centre " in the old limited sense, but that, being situated in the midst of other loci which control functions forming an integral part of the vomiting pattern, such as salivation or spasmodic respiratory movements, it acts as a co-ordinating mechanism. *J. B. Stanton*

2228. **The Effects of Sympathectomy on the Motility of the Human Gastrointestinal and Biliary Tracts**
J. R. Bingham, F. J. Ingelfinger, and R. H. Smithwick. *Gastroenterology* [*Gastroenterology*] **15**, Part I, 6–13, May, 1950. 1 fig., 11 refs.

Several methods were employed to study the effects of sympathectomy on the motility of the gastro-intestinal and biliary tracts of patients subjected to preganglionic sympathectomy for the treatment of hypertension.

In the study of the small intestine, balloon kymograph recordings of motility were obtained before and after operation on 19 patients. By this method volume changes are recorded in the intestinal balloon inflated under a pressure of 15 to 25 cm. of water. Two expressions of motility were observed: (*a*) Tone was recorded as the mean volume of air permitted to enter the balloon by the resistance of the bowel to distension. A 30% change in tone was considered significant. (*b*) Phasic

activity was shown as regular occurrence of small waves at the rate of 8 to 11 a minute, and large waves lasting for at least ½-minute and expelling at least 5 ml. of air from the balloon. A change in the frequency of these (propulsive waves) by 50% was considered significant.

The results show that in the early post-operative periods (up to 3 months) motility was clearly diminished; after this, slight increase was apparent. These changes in the early post-operative period may not be a specific effect of sympathetic denervation since similar changes were noted after operations other than sympathectomy. The effect may be due to spontaneous activity in the decentralized ganglia or to increased sensitivity of the bowel to circulating adrenaline.

Gastric and intestinal motility was also studied by means of a standard barium meal on 6 patients before and from 2 weeks to 1 year after operation. The only difference noted after sympathectomy was a slight delay in the transit of barium through the small bowel.

Histories were obtained from 300 consecutive patients who had undergone sympathectomy. In about one-fifth of the patients frequency of bowel movements had increased, but no other change was noted which might indicate an alteration in gastro-intestinal motor function. The gall-bladder took up dye and emptied satisfactorily in sympathectomized patients.

The common bile duct was perfused with physiological saline in 2 patients who had had both choledochostomy and bilateral sympathectomy. The pressure level at which neither salt solution passed into, nor bile flowed out of, the T-tube was used as an index of the resistance offered by the sphincter of Oddi and the duodenum. No significant change in the degree of this resistance was noted in the 2 cases.

The authors conclude that gastro-intestinal and biliary tract motility in man are not significantly changed by preganglionic sympathectomy. *M. Beaton*

2229. **The Effects of Sympathectomy on Abdominal Pain in Man**

J. R. BINGHAM, F. J. INGELFINGER, and R. H. SMITHWICK. *Gastroenterology* [*Gastroenterology*] **15**, Part I, 18–31, May, 1950. 4 figs., 15 refs.

The authors studied the induction of abdominal pain in man before and after unilateral and bilateral lumbo-dorsal sympathectomy. Pain was classified as arising from the oesophagus, duodenum, jejunum, ileum, colon, rectum, and biliary tract. In studies of the different parts of the intestine, pain was produced by inflating balloons placed in the respective parts of the intestine, and biliary-tract pain was induced by perfusing saline under pressure through a T-tube in the common duct.

Before sympathectomy oesophageal pain was felt substernally over the situation of the balloon in 25 out of the 27 cases studied. The remaining 2 patients had discomfort in the neck. Heartburn was not experienced by any, even in those subject to this symptom. Duodenal pain was typically situated in the upper epigastrium in the midline. Pain over the duodenum was produced by injecting an average of 54 ml. into the balloon. Jejunal and ileal pain was situated lower down in the abdomen, upper jejunal in the epigastrium and ileal in the peri-umbilical region. The average amount of air required to produce pain in the small intestine was 60 ml. Biliary-tract pain had the same situation and character as duodenal pain.

After unilateral sympathectomy, pain was referred to the side not operated upon in the case of the small intestine and biliary tract, and in some cases became more diffuse. This lateral reference varied in degree, depending on the part of the gut stimulated. It was most marked in the duodenum, less so in jejunum, and least in the ileum. After unilateral sympathectomy the pain threshold rose, so that greater distension was needed to produce the same intensity of pain in the intestine or biliary tract. The oesophagus was unaffected in this respect; this indicated that the change was not due to some possible central non-specific mechanism.

In all cases of bilateral sympathectomy involving the lower thoracic sympathetic chain and splanchnic nerves this pain was abolished. This was the case for all parts of the small intestine and the common duct. The oesophageal response was inconclusive. Colonic and rectal pain was studied in a few cases after bilateral sympathectomy. The results were not conclusive in the case of the caecum and ascending colon, but in the descending colon and sigmoid no pain was elicited after distension with 250 ml. of air (normal threshold being 50 ml.) after section of the splanchnics and removal of the sympathetic chain from D8 to L1. Rectum and sigmoid were sensitive to 50 ml. air even after lumbo-dorsal sympathectomy.

Regeneration of the pain pathways was not apparent 1 to 6 years after sympathectomy, but the authors note that this does not exclude regeneration at a later date than this. The raising of the pain threshold after unilateral sympathectomy affords an explanation of the relief of pain following this operation for disease of the pancreas, which is a bilaterally innervated organ. The localization of small-bowel pain to the unoperated side after unilateral sympathectomy supports the findings of other workers.

The results obtained by this study and by others of similar type serve a three-fold purpose: (1) The distribution and course of the visceral sensory nerves may be more precisely defined. (2) This information may be applied to determine the site and extent of any sympathectomy undertaken to relieve intractable pain arising in an abdominal viscus. (3) The difficulty of diagnosing abdominal disease in the sympathectomized patient is emphasized. *M. Beaton*

AVIATION MEDICINE

2230. **Studies on Airsickness**

B. A. STRICKLAND, G. L. HAHN, and H. ADLER. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **21**, 90–97 and 163, April, 1950. 15 refs.

By flying test-subjects in an aircraft in which the pilot manœuvred the machine to simulate the effects of passage through turbulent air, a realistic test for airsickness susceptibility was obtained. This method showed "dramamine" (β-dimethylaminoethylbenzhydryl ether 8-chlorotheophyllinate) to be effective in the prevention of

airsickness. Under similar conditions hyoscine hydrobromide in doses of 0·65 mg. was found to be about 10% better as an airsickness preventive. In these tests the distribution of subjects taking placebos and taking the test drug in the aircraft was carefully controlled. Studies on 20 susceptible subjects showed that dramamine was no more effective than the placebo in the prevention of swing sickness.

The side-effects of dramamine, of relatively minor degree, were found in only 8·7% of 206 recipients. The drug had no adverse effects on the ability to perform a complex co-ordination test or on reaction time. This latter finding was also true of hyoscine hydrobromide, and the only side-effect of the latter was some dryness of the mouth in 15% of 88 subjects.

The authors think that the terms vagotonia and sympathotonia were rarely applicable to subjects in these experiments.

[A good discussion of previous work on airsickness is included.] *K. E. Cooper*

2231. **Some Physiological Findings on Normal Men Subjected to Negative G**

E. A. Ryan, W. K. Kerr, and W. R. Franks. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **21**, 173–194, June, 1950. 8 figs., 12 refs.

Subjects were exposed to negative " g " on a tilt table and in the " human centrifuge ". The outstanding symptom on exposure up to −3 " g " was a feeling of pressure in the head; visual symptoms were common at the higher values. Bradycardia was noted and was proportional to the amount of negative " g "; this was considered to be due to the carotid sinus reflex. The pulse rate quickly returned to normal when the acceleration passed off. The bradycardia was more marked on subsequent than on initial exposures; this fact was correlated with subjective increase in tolerance to the acceleration. Electrocardiograms taken during the exposure showed prolonged periods of cardiac asystole. *D. H. Sproull*

2232. **Effects of Positive Acceleration on Pilots in Flight, with a Comparison of the Responses of Pilots and Passengers in an Airplane and Subjects on a Human Centrifuge**

E. H. Lambert. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **21**, 195–220 and 250, June, 1950. 12 figs., 18 refs.

The responses to positive " g " of 16 men piloting a dive bomber were compared with their own responses as passengers in the aeroplane, and in the centrifuge. When piloting, vision was dimmed, lost peripherally, and lost completely at averages of 4·6 " g ", 5·0 " g ", and 5·4 " g " respectively. Loss of ear pulsation occurred at 5·3 " g ". These values are 0·7 " g " higher than the " g " tolerance of the subjects as passengers in the aeroplane and 1·4 " g " higher than those in the centrifuge. The higher " g " tolerance of pilots is attributed to posture, lower temperatures in the cockpit, and the effort of controlling the aeroplane. The cardiovascular responses of the pilots and passengers were similar, but differed from those of the subjects in the centrifuge. In the centrifuge pulse rates before and during acceleration were slower, and the compensatory reactions occurred one or two seconds later, than in the aeroplane. There was striking similarity in the visual and general symptoms, irrespective of the type of exposure. *D. H. Sproull*

2233. **Effect of Various Drugs on Psychomotor Performance at Ground Level and at Simulated Altitudes of 18,000 Feet in a Low Pressure Chamber**

H. F. Adler, W. L. Burkhardt, A. C. Ivy, and A. J. Atkinson. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **21**, 221–236, June, 1950. 4 figs., 7 refs.

The effect of several analeptic drugs on the psychomotor performance, pulse rate, vital capacity, visual flicker-fusion frequency threshold, auditory acuity range, and subjective symptoms of 16 subjects were studied at ground level, and at a simulated altitude of 18,000 ft. (5,400 m.), without supplementary oxygen. All the drugs improved the performance at altitude; D-amphetamine was the most effective, and L-amphetamine ranked next. Caffeine sodium benzoate was effective, but did not compare well with the amphetamines. Repeated exposure to altitude had no effect on the high and low frequency auditory range of the subjects, but measurement of the flicker-fusion frequency threshold revealed a gradual deterioration, which was correlated with an increasing feeling of fatigue. *D. H. Sproull*

2234. **The Immediate and Accumulative Effect on Psychomotor Performance of Exposure to Hypoxia, High Altitude and Hyperventilation**

J. Sców, L. R. Krasno, and A. C. Ivy. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **21**, 79–81, April, 1950.

Psychomotor performances of subjects, who were repeatedly exposed to altitude anoxia and hyperventilation, were measured. The tests used were: (1) Measurement of flicker-fusion frequency threshold. (2) Use of a device in which the subject followed the movement of an irregular slot in a revolving drum by means of a pointer—the " pursuitmeter ". Touching the side of the slot with the pointer electrically actuated a scoring device. (3) Use of a tremor detector. (4) Measurement of the rate at which a flat metal plate could be tapped with a pointer.

Performance deteriorated during a state of anoxia, but repeated exposure caused no progressive deterioration. Subjects became more irascible during repeated exposures to high altitude.

Daily repetition of one hour's hyperventilation in 7 subjects led to no accumulation of fatigue. No progressive deterioration in performance occurred in 7 subjects exposed to an altitude of 35,000 ft. (10,500 m.) while breathing 100% oxygen three times a week for 5 weeks. The performance was not decreased during individual runs. *K. E. Cooper*

2235. **Physiological Considerations regarding Safety Measures for Sudden Decompression in Civil Passenger Aircraft**

H. Whittingham. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **21**, 246–250, June, 1950. 1 fig.

Pharmacology and Therapeutics

2236. **The Antagonism Between Acetylcholine and the Curare Alkaloids, D-Tubocurarine, c-Curarine-I, c-Toxiferine-II and β-Erythroidine in the Rectus Abdominis of the Frog**

E. F. VAN MAANEN. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **99**, 255–264, June, 1950. 5 figs., 11 refs.

Experiments were performed on the excised rectus abdominis muscle of *Rana pipiens*. The only effect of the above alkaloids on the dose-response curve for acetylcholine was to shift the curve along the dose-scale; the maximal contracture which could be obtained with acetylcholine was not less in the presence of the antagonist. The antagonism was therefore considered to be competitive. By applying the law of mass action, the author derives the expression: $K_c = \frac{[C]\,[A]}{[A']-[A]}$, where [C] is the molar concentration of the curare-like agent, [A′] the molar concentration of acetylcholine producing 50% of the maximal contracture of the muscle in the presence of the antagonist, and [A] the molar concentration of acetylcholine producing 50% of the maximal contraction when no antagonist is present. For the three quaternary alkaloids tested, the "activity constant" (K_c) was independent of the concentration of alkaloid used. It was further shown in the case of D-tubocurarine that variation of the temperature between 5° C. and 35° C. or of potassium ion concentration between 1 and 8 mM. per litre did not alter significantly the K_c value. [This activity constant may prove as useful for comparing antagonist activity as the pA_x index of Schild (*Brit. J. Pharmacol.*, 1947, **2**, 189.]

F. N. Fastier

2237. **Studies on the Blood–Brain Barrier. II. Attempts to Influence the Passage of Substances into the Brain**

E. W. HURST and O. L. DAVIES. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 147–164, June, 1950. 31 refs.

The authors investigated the effects in mice of a variety of agents on the uptake by the brain of (*a*) 14 different dyes (measured by comparing the colour of fixed sections with standard colour-washes on paper); (*b*) the convulsant drugs strychnine, picrotoxin, and cocaine (as judged from the mortality); (*c*) morphine (as judged from its analgesic effect); and (*d*) sulphanilamide and sulphanilic acid (determined chemically). [The original should be consulted for details of the techniques used.]

Of the agents tested only 50% glycerol (1 ml. given intravenously) produced a consistent effect, increasing the uptake of all the test substances. Adrenaline and pituitary extract (together), "theocin" (theophylline sodium acetate), and histamine increased the mortality from all the convulsants, increased the analgesic effect of morphine, and caused some of the dyes to penetrate more rapidly. Sodium lactate increased the mortality from the convulsants, but did not influence the effect of morphine or the penetration of the dyes. Urethane diminished the effect of picrotoxin and strychnine and the penetration of two of the dyes, but increased the effect of cocaine. Coal-gas poisoning and ether anaesthesia increased the penetration of those dyes which normally penetrate readily. Trypan red diminished the mortality from the convulsants, but had no effect on morphine. Neutral-red chloride and brilliant vital red produced very inconclusive and contradictory results. Hexamine diminished the toxicity of the convulsants and did not affect the penetration of morphine or the dyes. The penetration into the brain of sulphanilamide and sulphanilic acid [the only substances whose concentrations in the brain were accurately determined] was affected by few of the agents used. Penetration of both was increased by glycerol, hexamine and ether anaesthesia increased the penetration of sulphanilic acid, but not of sulphanilamide, and coal-gas inhalation increased the passage into the brain of sulphanilic acid and diminished that of sulphanilamide.

R. P. Stephenson

2238. **Effects on Anaphylactic Shock of Salicylates, Aminopyrine and Other Chemically and Pharmacologically Related Compounds**

M. H. LEPPER, E. R. CALDWELL, P. K. SMITH, and B. F. MILLER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 254–258, June, 1950. 18 refs.

Oral administration to sensitized rabbits of 0·64 g. of acetylsalicylic acid or 0·57 g. of sodium salicylate reduced markedly the percentage mortality caused by intravenous injection of 2 ml. of egg-white, one hour later. A still greater protective effect was given by 0·82 g. of aminopyrine. None of these drugs had any effect on sensitivity to histamine. A number of related compounds, given in equimolar doses, had no protective effect. It is suggested that the effective compounds inhibit the combination of antigen and antibody.

V. J. Woolley

2239. **Intravenous Administration of Tetracaine ("Pontocaine") Hydrochloride. Preliminary Report**

J. S. HORAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **85**, 972–979, June, 1950. 5 refs.

The author treated 104 patients, mostly workers from a sugar plantation or patients in a leprosy treatment centre in Hawaii, with a total of 204 intravenous injections of "tetracaine" (butethanol, *B.P.*, "pontocaine") for the relief of pain, itching, asthma, and miscellaneous conditions. An infusion of 10 ml. of 0·25% tetracaine hydrochloride solution was given slowly intravenously over a period of 3 to 5 minutes. The patient was kept supine during this time and for 5 minutes afterwards. Satisfactory results were obtained in cases of asthma,

arthritis, the " deep " itch of leprosy, low back pain, muscle strain, hyperactive carotid-sinus syndrome, neuritis, and various other conditions causing aching and itching. Analgesic, antispasmodic, and antihistaminic properties are claimed for this drug, which is said probably to have a selective affinity for inflamed or traumatized tissue. The only toxic reactions observed were slight nausea in one patient and syncope in another. Increased excitement, talkativeness, restlessness, muscular twitching, skin reactions, or dyspnoea during the administration of tetracaine should be regarded as indications for the immediate cessation of the injection.

I. Ansell

2240. **Neostigmine and Opiate Analgesia.** [In English] D. SLAUGHTER. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **83**, 143–148, 1950. 8 refs.

It was reported 9 or 10 years ago that the analgesic effect of morphine was potentiated by neostigmine in cats and in human subjects. Others have since confirmed this observation. As a result of experiments on human volunteers with a modified Hardy, Wolff, and Goodell radiant-heat method for testing analgesia, it is now shown that otherwise non-effective doses of morphine and codeine have considerable analgesic activity when injected intramuscularly together with 0·5 mg. of neostigmine. The effects of " dilaudid " and " pantopon " were also increased. A particularly striking effect was seen with codeine, 32 mg. of codeine phosphate and 0·5 mg. of neostigmine having a much greater effect than 64 mg. of codeine alone. The neostigmine also reduced the muscular weakness and other side-effects due to morphine and dilaudid. The mechanism of the potentiation is uncertain.

Derek R. Wood

2241. **Analgesic Action of 3-Hydroxy-N-methyl Morphinan Hydrobromide (Dromoran)**
L. O. RANDALL and G. LEHMANN. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **99**, 163–170, June, 1950. 4 figs., 11 refs.

" Dromoran " is a synthetic substitute for morphine and lacks only the ether-oxygen bridge of dihydrodesoxymorphine-D. It approaches morphine in structure more closely than does methadone. The analgesic activity of this new compound, given to rats by the subcutaneous route, was four times as great as that of morphine and the duration of action was considerably longer. By the oral route dromoran was about 1·5 times as potent as methadone and longer in duration of action. Analgesic action was tested by measuring the reaction time, that is, the time elapsing until the appearance of skin twitch when a heat stimulus is applied to the shaved back. Tolerance to analgesia was also measured in rats. Giving daily subcutaneous doses of 3 mg. of dromoran per kg. and of 6 mg. of morphine per kg. indicated that tolerance developed at about the same rate.

Respiration of non-anaesthetized rabbits was decreased by doses of dromoran about one-fourth those of morphine, and the duration of this action was longer. The effect on intestinal motility was measured on trained non-anaesthetized dogs with a Thiry–Vella fistula of the jejunum. Dromoran (1 mg. per kg. intravenously) increased motility to the same extent as did morphine at a dose level of 2 mg. per kg. It was six times (LD 50 41 mg. per kg.) as toxic to rats as morphine when given intravenously, and about five times as toxic subcutaneously. Compared with methadone, however, it was about one-half as toxic by both routes. In chronic toxicity studies, characteristic morphine effects in animals were noted. These included tail erection in mice, excitement in cats, depression in dogs, and catatonia in rats. The safety factor (ratio of acute toxicity to analgesic activity) is equal to or slightly less than that for morphine but at least twice that for methadone. Practically all the analgesic and respiratory depressant action of the racemic mixture (dromoran) is attributable to the *laevo*-isomer. This compound possesses certain important advantages over those of morphine.

G. B. West

2242. **The Site of Action of Phenergan and Neoantergan on Body Temperature and Oxygen Consumption in Normal and Adrenalectomized Rats**
D. R. WOOD. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 195–203, June, 1950. 6 figs., 7 refs.

The antihistamine substances, " antergan ", " neoantergan ", and " phenergan ", are known to cause a fall in body temperature. In the investigation reported here the oxygen consumption of rats before and after injection of the last two drugs was measured by the method of Bargeton and Krumm-Heller and rectal temperature changes also noted. The injection of phenergan (5 mg. per 100 g. body weight) produced a fall in body temperature accompanied, after a slight rise, by a fall in oxygen consumption. The fall often occurred during a period of increased muscular activity and was probably central in origin. Adrenalectomy increased both effects, which were also greater in rats which were usually kept at fluctuating environmental temperatures than in rats kept since birth at 29·5° C., at which temperature all experiments were performed. Neoantergan also showed signs of a central depressant effect on heat regulation, though this was overshadowed by convulsions. The phenothiazine compound, " 3,300 R.P.", although similar in structure to phenergan, has no antihistamine activity and did not depress body temperature or oxygen consumption.

R. P. Stephenson

2243. **The Cardiovascular Effects of the Intranasal Administration of Acetyl-β-methylcholine Chloride (Mecholyl)**
M. H. NATHANSON, J. TOBER, and H. MILLER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **219**, 639–647, June, 1950. 10 figs., 6 refs.

In 14 hypertensive patients, the blood pressure and pulse rate were measured before and at 30-second and 60-second intervals after the subcutaneous injection of 25 mg. doses of " mecholyl ". In several, electro-

cardiographic records were also obtained. The onset and intensity of the systemic effects were noted. Similar observations were then made in the same patients after application to the nasal mucosa for about 2 minutes of a pledget of cotton wool saturated with a solution of 200 mg. of mecholyl in water. The depressor responses were as great, or even greater, with the latter technique, though somewhat less prolonged. The amount of the drug absorbed in the second series could not be gauged, and so no comparison could be established between the actual doses needed to produce the same effect in the two series.

In a further 6 hypertensive patients a similar set of observations was made after: (*a*) the subcutaneous injection of 20 mg. of mecholyl; (*b*) the application, by dropper, of 50 mg. of the drug in aqueous solution to the nasal mucosa under conditions which should have led to complete absorption. In 5 of the patients the systemic effects were very similar in onset and intensity with both methods of administration, while in the sixth the subcutaneous injection produced more marked action. It is estimated, therefore, that the dose for intranasal administration should be 2·5 to 3 times as great as that by subcutaneous injection.

Electrocardiographic records show a variety of effects on the heart produced by mecholyl. In no case was there need to administer atropine to check excessive action. The authors suggest that the intranasal application of mecholyl may have some place in treatment of heart disease. They report that no effects followed the sublingual application of tablets of acetyl-β-methylcholine iodide, with or without the addition of neostigmine. *Reginald St. A. Heathcote*

2244. **The Effects of Digoxin and Ouabain on the Heart–Lung Preparation of the Dog**

J. M. WALKER, E. M. LOURIE, and J. H. BURN. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 306–314, June, 1950. 4 figs., 10 refs.

McMichael (*Brit. med. J.*, 1948, **2**, 927), using a method of right heart catheterization, was led to conclude that while ouabain had a direct stimulating action on the heart the beneficial effect of digoxin was mainly due to a reduction in venous pressure. The present authors compared the actions of ouabain and digoxin on the Starling heart–lung preparation of the dog. The preparations were either allowed to deteriorate spontaneously, or heart failure was accelerated by the continuous addition of thiopentone or pentobarbitone to the blood in the venous reservoir. Cardiac output and sometimes right auricular pressure or the outflow from the coronary sinus were recorded. Ouabain was given to 12 dogs in doses of 0·1 mg. (9 experiments), 0·15 mg. (2 experiments), and 0·2 mg. (1 experiment). In all these experiments the cardiac output was increased, the mean percentage increase for those given 0·1 mg. ouabain being 25% (ranging from 9% to 37%). Digoxin (0·2 mg.) appeared to have a similar effect; in 8 experiments the mean percentage increase in cardiac output was 20% (ranging from 1% to 41%).

These results are discussed in relation to those of McMichael and others; it is concluded that both ouabain and digoxin have a direct action on heart muscle under the experimental conditions and that the action in man is probably similar. [The percentages quoted above do not do justice to the experimental results: reference to the original paper will show the details of each experiment. The results recorded in both the above papers, and obtained in different ways, support the view that the cardiac glycosides do, in fact, stimulate the heart. It becomes increasingly difficult to accept the explanation given by McMichael.] *John R. Vane*

2245. **Effect of Digitalis on the Clotting of the Bood in Normal Subjects and in Patients with Congestive Heart Failure**

R. T. CATHCART and D. W. BLOOD. *Circulation* [*Circulation*] **1**, 1176–1181, May, 1950. 13 refs.

An earlier claim that digitalis favours coagulation of the blood suggested that it would be interesting to investigate such a possible action in normal subjects and in patients with congestive heart failure. Clotting times were measured by a modification of the Lee–White method and by the Leifer method. Prothrombin times were measured by an adaptation of Quick's method on undiluted plasma and on plasma diluted eight times with 0·9% saline solution. Blood samples were tested before and for 5 days after starting the administration of digitoxin, lanatoside-C, or digitalis leaf, *U.S.P.* XII. Another group of hospital patients did not receive digitalis and were used as controls, on whom repeated estimations of clotting time and prothrombin time were made.

No consistent changes either in clotting or prothrombin time were found after digitalization, and the average changes were small and statistically insignificant from those occurring in the control patients not given digitalis. *Derek R. Wood*

2246. **Antispasmodic Drugs. Evaluation of their Effects on the Motor Activity of the Upper Portion of the Small Intestine in Man**

W. P. CHAPMAN, E. N. ROWLANDS, and C. M. JONES. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 627–630, June 17, 1950. 4 figs., 9 refs.

Motor activity in the jejunum of human subjects was recorded kymographically by means of a series of 4 balloons connected by a 4-lumen tube to a water manometer. It was found that giving inert substances by mouth caused a small reduction in the size and number of propulsive contractions occurring in the jejunum. Oral administration of atropine, 0·6 mg., and tincture of belladonna, 0·4 ml., produced an 80% reduction in intestinal activity between 1 and 2 hours later. Certain synthetic antispasmodic drugs, including "pavatrine", "asymatrine", amphotropine ("syntropan"), and "trasentin" were tested and found not to produce any lessening of intestinal activity.

The authors publish scatter-diagrams and emphasize the extreme variability in intestinal motility from subject to subject and in the same subject from hour to hour, and the variations in the response of different individuals to atropine and the other drugs. Nevertheless, atropine

caused an average decrease in activity of 50% more than that occurring after the administration of inert substances. *John Naish*

2247. **Histamine Antagonists. XV. Comparative Experimental Studies of Certain Antihistaminic Compounds**
S. M. FEINBERG, S. MALKIEL, T. B. BERNSTEIN, and B. J. HARGIS. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **99**, 195–201, June, 1950. 8 refs.

The activities of a series of 26 selected histamine antagonists were compared by four biological tests. In the first, guinea-pigs received intraperitoneal doses of 0·1 and 1·0 mg. per kg., and after 30 minutes one lethal dose of histamine (0·4 mg. per kg.) was given intravenously to each. Deaths from histamine shock were recorded and the findings compared with those in experiments on anaphylactic shock. In the latter tests guinea-pigs were given an intraperitoneal injection of 1 ml. of a 1 in 10 dilution of horse serum; after 14 days an intravenous injection of 1 ml. of undiluted horse serum was given 30 minutes after the intraperitoneal injection of the antihistaminic drug. Doses considerably greater than 1·0 mg. per kg. were needed to afford protection against the fatal anaphylactic shock. In the third test suitable guinea-pigs were placed in a chamber filled with histamine aerosol 30 minutes after the intraperitoneal injection of a given drug. The end-point adopted was 10 minutes' exposure without dyspnoea. In the fourth test guinea-pigs were subjected to the action of aerosols of varying concentrations of the antihistaminic drugs for 5 minutes, after which they were exposed to the histamine aerosol. By these four tests tripelennamine (" pyribenzamine ") hydrochloride and " chlorneoantergan " were found to be the most active of all the compounds. *G. B. West*

2248. **Pharmacology of β-Diethylaminoethyl Xanthene-9-carboxylate Methobromide (Banthine) and Chloride**
W. E. HAMBOURGER, D. L. COOK, M. M. WINBURY, and H. B. FREESE. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **99**, 245–254, June, 1950. 6 figs., 15 refs.

The main pharmacological actions of " banthine " resemble those of atropine. It reduced intestinal motility and tone in the cat and dog, and antagonized the effect of acetylcholine on isolated rabbit intestine; it dilated the rabbit's pupil when applied locally; it reduced salivary secretion in the dog; it antagonized the depressor action of acetyl-β-methylcholine (" mecholyl ") in the dog and cat; and it prevented cardiac arrest due to vagal stimulation. On a molar basis, banthine has about $\frac{1}{2}$ to $\frac{2}{3}$ of the spasmolytic potency of atropine.

Slightly larger doses of banthine also blocked autonomic ganglia. Thus, although banthine did not antagonize the effect of adrenaline on the cat's nictitating membrane, it produced on intravenous injection a temporary relaxation of the sustained maximal contraction of the membrane caused by stimulating the craniad stump of the vago-sympathetic nerve trunk. On a molar basis its action on this preparation was about twice as powerful as that of tetraethylammonium bromide. With near-lethal doses of banthine a curare-like action became apparent. Death appeared to be due to respiratory paralysis. *F. N. Fastier*

2249. **Influence of Diphenhydramine on Blood Pressure Response to Epinephrine in the Dog under Adrenergic Blockade**
G. CHEN and D. RUSSELL. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 298–302, June, 1950. 2 figs., 17 refs.

In dogs anaesthetized with pentobarbitone, injection of 20 mg. of diphenhydramine per kg. restores to a slight degree the vasopressor action of adrenaline which has been reversed by administration of the adrenergic blocking agent, N-(2-bromoethyl)-N-ethylnaphthalene methylamine hydrobromide. A similar but lesser effect is produced if adrenaline is replaced by arterenol. Among other drugs examined, all those which potentiate adrenaline act in the same way as diphenhydramine, but atropine, papaverine, and antihistaminic drugs have no such effect. *V. J. Woolley*

2250. **Response of Circulation Eosinophils to Norepinephrine, Epinephrine and Emotional Stress in Humans**
R. J. HUMPHREYS and W. RAAB. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.,*] **74**, 302–303, June, 1950. 16 refs.

Subcutaneous injection of 0·25 mg. of adrenaline caused an average decrease of 61% in the eosinophil count in 12 subjects. The same dose of L-noradrenaline caused a decrease of 9%. In 24 students the eosinophil count was 66 per c.mm. just before an examination and 128 per c.mm. several weeks later. *V. J. Woolley*

2251. **Eosinophil Response to Epinephrine and Norepinephrine**
P. C. PELLEGRINO, G. M. MORRIS, and S. TRUBOWITZ. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 330–332, June, 1950. 2 figs., 9 refs.

Intravenous administration of 0·2 and 0·3 mg. of L-noradrenaline to 20 and 6 patients respectively caused a significant fall in the eosinophil count in only 2 of the 20 and 1 of the 6. It is suggested that these falls were due to emotional disturbance through the experiment and not to the drug. *V. J. Woolley*

2252. **Absorption, Distribution and Excretion of Phenindamine (Thephorin)**
R. E. DAILEY, E. L. WAY, J. R. PARIKH, CHEN-YU SUNG, and D. L. HOWIE. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 394–398, June, 1950. 2 figs., 4 refs.

The antihistaminic substance phenindamine (2-methyl-9-phenyl-2 : 3 : 4 : 9-tetrahydro-1-pyridindene) can be determined in tissue extracts by the Brodie–Udenfriend method if the benzene extract is washed four times with an acetate buffer at *p*H 5·5. After oral administration to man only traces are present in the urine. When given by stomach tube to rats 75% disappears from the

alimentary canal in 4 hours, but 10% is present after 24 hours. When given intraperitoneally to rats it becomes mainly localized in the lungs, liver, kidneys, and spleen. Some is in the brain but none in heart or muscle. In rats which received 20 mg. of phenindamine per kg. twice daily for 4 days none could be found in the tissues 24 hours after the last dose. It is concluded that it is rapidly absorbed and metabolized in the body.

V. J. Woolley

2253. **Studies on the Inter-relationships of Certain Cholinergic Compounds. III. The Reactions between 3-Acetoxy Phenyltrimethylammonium Methylsulfate, 3-Hydroxyphenyltrimethylammonium Bromide and Cholinesterases**

W. C. Wescoe, W. F. Riker, and V. L. Beach. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **99**, 265–276, June, 1950. 7 figs., 24 refs.

"Nu 2017", 3-acetoxy phenyltrimethylammonium-methyl sulphate, closely resembles acetylcholine in its pharmacological properties. Its effects are almost equally brief, probably because it is hydrolysed almost as rapidly as acetylcholine. Hydrolysis of Nu 2017 is soon appreciable even in aqueous solution, especially if this be alkaline. The hydrolysis is catalysed by the cholinesterases of serum, erythrocytes, and brain, as indicated by *in vitro* experiments. (All determinations of cholinesterase activity were made by slight modifications of Ammon's method with the standard Warburg manometric technique.) The hydrolysis product of Nu 2017, 3-hydroxyphenyltrimethylammonium ("Nu 2561"), inhibits erythrocyte cholinesterases to the same extent as Nu 2017 when present in equimolecular concentrations. Since it was found by the method of Lineweaver and Burk that the inhibition of serum cholinesterases by Nu 2561 is of the competitive variety, it is deduced that the parent compound, Nu 2017, is also a competitive inhibitor of cholinesterases. The authors consider that the competitive inhibition which they have demonstrated *in vitro* also occurs *in vivo*, but that the pharmacological effects of Nu 2017 and of Nu 2561 are brought about mainly by direct action. *F. N. Fastier*

2254. **Further Studies on Sympathin**

G. B. West. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 165–172, June, 1950. 3 figs., 35 refs.

The different effects of adrenaline and noradrenaline on the uterus, blood pressure, and nictitating membrane of the cat were used as a means of determining the nature of various sympathins. The experiments were performed either on single cats under chloralose and cocaine and after double vagotomy, the agent being carried from the liberating to the test organ by the intact circulation, or on a pair of cats, samples of venous blood being collected from one animal and injected into the arterial supply of the test organ in the other cat.

The effects of splanchnic-nerve stimulation corresponded to the infusion of adrenaline alone, equiactive effects on uterus, blood pressure, and nictitating membrane being obtained. After cutting the splanchnic nerves, the effect of stimulation could be matched by adding an increasing proportion of noradrenaline to the infusion with the adrenaline. Stimulation of the recently sectioned hepatic nerve could be matched by the intraportal infusion of mixtures of adrenaline and noradrenaline, but after a longer interval noradrenaline alone was sufficient. The intraportal injection of 2-benzyl-1-methylimidazoline, which potentiates the pressor action of adrenaline, had no such effect when noradrenaline was injected, or on hepatic-nerve stimulation. Stimulation of the splenic nerve produced a small effect on the circulation which was matched by injection of 0·1 μg. of noradrenaline, and the result of injection of blood taken from the splenic vein after stimulation into the arteries of a second cat indicated that noradrenaline in a concentration of 0·2 to 0·66 μg. per ml. was released by stimulation. The non-pregnant uterus was relaxed by both adrenaline and noradrenaline injected either intravenously or into the external iliac artery, whereas in pregnant animals the effects of both were excitatory. Stimulation of the hypogastric nerve produced similar effects. It was thus not possible to identify the uterine sympathin. *R. P. Stephenson*

2255. **The Nature of Hepatic and Splenic Sympathin**

M. Mann and G. B. West. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 173–177, June, 1950. 2 figs., 9 refs.

Blood was collected from the hepatic and splenic veins of cats anaesthetized with chloralose. A loop of thread was passed round the inferior vena cava between the liver and the adrenal glands and another just above the diaphragm. Samples of 5 ml. of blood from the hepatic vein were withdrawn with a syringe and needle from a small pocket formed at the opening of the hepatic vein into the vena cava when the threads were extended. Heparin was injected intravenously and the blood samples were immediately centrifuged in cooled tubes. The adrenal vessels were ligated in some experiments. The hepatic nerve was dissected free from the artery and faradic stimulation applied for 1 minute. The plasma from two samples taken during stimulation was added to that from one taken immediately after. Control plasma was obtained from samples of hepatic-vein blood taken before and 10 minutes after stimulation. Splenic venous blood (3 to 6 ml.) was collected from a cannula in the splenic vein during and for 2 minutes after stimulation of the splanchnic nerve; when not being collected the blood was returned to the femoral vein. The plasma samples were assayed on (1) isolated uterus, from a rat in dioestrus, sensitive to concentrations of 10^{-10} of adrenaline or 5×10^{-9} of noradrenaline; (2) isolated rectum from the week-old chick sensitive to 5×10^{-10} of adrenaline and 10^{-8} of noradrenaline; and (3) chronically denervated nictitating membrane of a cat under chloralose anaesthesia, giving contractions with either adrenaline or noradrenaline in concentration of 10^{-8}. When mixtures of the two amines were added to plasma, each could be accurately estimated. [It is stated that as little as 4% of one amine could be accurately estimated in a mixture of the two, but no evidence is given to support this rather surprising claim.]

The hepatic venous samples taken during stimulation contained noradrenaline in amounts varying from 0·05 μg. per ml. to 0·66 μg. per ml. in 10 experiments when the blood supply to the adrenals was tied off, and 1·0 μg. per ml. in 3 experiments when the adrenals were still in the circulation; adrenaline was detected only twice, in concentrations of 0·002 μg. and 0·003 μg. per ml. respectively. In 15 experiments with splenic venous blood stimulation produced 0·05 μg. to 0·30 μg. per ml. of noradrenaline, with 0·10 μg. per ml. of adrenaline in one case, and less than 0·002 μg. per ml. of adrenaline in all other cases. Tying off the adrenals did not affect the concentrations in the splenic samples. The presence of noradrenaline and the complete or virtual absence of adrenaline was confirmed by the effects of the samples on the rat uterus; in full oestrus, adrenaline, noradrenaline, and the sample all produced contractions, whereas in early oestrus the sample and noradrenaline produced contractions, but adrenaline caused inhibition.

R. P. Stephenson

2256. **Treatment of Parkinsonism with "Rigidyl".** (Behandling af Parkinsonisme med Rigidyl)
M. Fog. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **112**, 748–750, May, 25, 1950.

The author treated 14 cases of Parkinsonism, including 5 of post-encephalitic Parkinsonism and 2 of arteriosclerotic muscular rigidity, with "rigidyl" (β-diethylaminoethylbenzhydryl ether hydrochloride), which differs from "benadryl" in having two ethyl groups substituted for the methyl groups. In 3 cases the condition was graded clinically as severe, in 9 as moderately severe. In 6 of the cases the outstanding feature was rigidity. Nine cases showed definite improvement, rigidity being diminished and mobility increased, but tremor was unaffected; these patients had previously been treated with belladonna alkaloids, but preferred rigidyl. Clinical improvement was most marked in the most severely affected patients. Treatment was begun with a dose of 100 mg. daily, increasing to 4 times daily; when improvement was evident the dose was altered to 50 mg., 150 to 300 mg. a day usually being found sufficient. Diminution of rigidity was evident about half an hour after each dose. Mild and transient symptoms of intolerance occurred in the first few days in some cases. Drowsiness and atropine-like side-effects were not observed. Treatment had to be discontinued in 3 cases after a few days and in one case after 5 weeks because of nausea, dizziness, or conjunctival irritation.

John Foley

2257. **Pharmacology of "Rigidyl" (β-Diethylaminoethylbenzhydryl ether).** (Bidrag til β-diaetylaminoaetylbenzhydrylaeters (rigidyl) farmakologi)
V. Larsen. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **112**, 750–753, May 25, 1950. 2 figs., 2 refs.

Study of the pharmacological action of "rigidyl" (β-diethylaminoethylbenzhydryl ether hydrochloride), which is similar in structure to "benadryl" except for the substitution of two ethyl groups in place of the methyl groups of the latter, showed that it is very slightly more toxic than benadryl for mice. It was found that the qualitative effect of the two compounds on strips of guinea-pig small gut was the same, but there were quantitative differences. The concentrations of the two substances required to effect an 80% reduction in the contraction caused by histamine, acetylcholine, and barium chloride were determined. The antihistaminic action of rigidyl was four to five times less than that of benadryl, while its atropine-like effect was two to three times greater. The degree of inhibition was found to depend not on the absolute concentration of the compound, but on the ratio between the concentration of the inhibitory substance and the concentration of the agent causing smooth-muscle contraction. The papaverine-like effect, as tested against barium chloride, was about the same with both compounds; there was no definite relation in this case between the concentrations of the two substances. Although the atropine-like action of rigidyl was thus demonstrated in these experiments, atropine side-effects such as paresis of accommodation and dryness of the mouth are not associated with its clinical use.

John Foley

2258. **Intravenous Thrombokinase Therapy.** (Zur intravenösen Thrombokinasetherapie)
F. Leonhartsberger and J. Schmid. *Wiener Klinische Wochenschrift* [*Wien. klin. Wschr.*] **62**, 437–443, June 23, 1950. 3 figs., 28 refs.

A protein-free phospholipid fraction was prepared from calf brain. It can be injected intravenously without untoward reaction. On such injection it will reduce clotting time but has no effect on prothrombin time; it is therefore theoretically more suitable for use in cases of the haemophilic group with thrombokinase deficiency or circulating antithrombin than in cases of hypoprothrombinaemia. A series of 78 cases of haemorrhage from various sites, mostly in subjects without blood disease, were treated with alleged benefit. Some details are given of 25 cases in which adequate haematological control was possible and in all of which there was some reduction in clotting time, although in most cases this was slight; the therapy was thought to have been instrumental in stopping the bleeding. *P. C. Reynell*

2259. **The Effect of Phenylindanedione on Plasma Prothrombin and Factor V Levels and a Comparison with the Effect of Dicumarol**
C. J. Bjerkelund. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **2**, 83–91, 1950. 9 figs., 9 refs.

Of various indanedione derivatives, 2-phenylindane-1 : 3-dione (P.I.D.) was the most active in its effect on prothrombin and factor-V concentrations in blood. (For factor-V determination plasma from a parahaemophiliac (lacking the factor) was used instead of the prothrombin and fibrinogen reagents used originally.) Single oral doses of 200 mg. were given to fasting subjects; blood samples were taken 12-hourly for 72 hours and then daily until the original prothrombin value was attained. In 9 patients, prothrombin levels fell for 12 hours, with a maximum fall at 24 to 36 hours of 53

to 87% (mean 68%). A rapid rise to the original level occurs over 72 to 120 hours after beginning the experiment.

The work was repeated on 11 patients, 5 receiving 50 mg. vitamin K intravenously and 6 receiving 50 mg. orally daily; the fall in prothrombin content was significantly reduced by intravenous doses of the vitamin from 28 to 41% (mean 37%). Results were less uniform when vitamin K was given by mouth. Phenylindanedione, in single doses, had no effect on factor-V concentration, with or without concomitant vitamin-K administration.

Doses of 200 to 300 mg. per day by mouth given to patients with thrombo-embolic diseases caused a rapid uniform fall in prothrombin value (10 to 20% in 2 days), the low level being maintained by 100 mg. P.I.D. per day, in undivided doses. Cessation of P.I.D. therapy resulted in return to normal of prothrombin level in a few days. No toxic reactions or complications of any kind were observed. *Malcolm Woodbine*

2260. **The Pharmacology of Thiomerin**

R. A. LEHMAN, E. E. KING, and H. TAUBE. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **99**, 149–162, June, 1950. 5 figs., 18 refs.

The pharmacological properties of thiomerin were studied and compared with those of mercurophylline *U.S.P.*, mersalyl with theophylline *U.S.P.*, and " mercuhydrin ". Thiomerin (mercaptomerin sodium) is a mercurial diuretic in which the theophylline residue commonly present in these drugs has been replaced by a monothiol. Its acute systemic toxicity was studied in mice, rabbits, and cats. The lethal dose in mice when measured at 30 minutes after injection was about twenty times that of mercurophylline, but when measured at 96 hours was about the same; a similar result was obtained in the rabbit and cat. On the isolated cat heart, however, thiomerin was about twenty times less toxic than was mercurophylline. There was no significant difference in the toxicity of thiomerin in mice when given by the subcutaneous and intravenous routes.

In a chronic toxicity test on dogs the effects of subcutaneous doses of thiomerin, equivalent to 4 mg. of metallic mercury per kg. body weight, given three times a week, were compared with those of a similar equivalent dosage of mercuhydrin over a period of 3 months. There were no significant changes in the blood picture or the body weight, but degenerative changes in the liver cells were observed in both groups. The same two substances were given intravenously (in half the above doses) to rabbits three times a week for 30 days. At necropsy there was no significant difference in the histological findings in the kidney and liver in the two groups, the main features being cloudy swelling of the tubular epithelium and of the hepatic cells. Analysis of the kidneys for their mercury content indicated a greater retention in the group given thiomerin than in that given mercuhydrin. Little difference was observed, however, in the rate of absorption of the two substances from the tibialis anterior muscle of the rabbit.

The excretion of mercury by patients with heart disease was studied after the administration of each of the above drugs (except mercuhydrin) in doses equivalent to 80 mg. of metallic mercury. The average recovery of mercury in each case was about the same, as was the rate of excretion of chloride. Therefore it would appear that by structural modification of the common mercurial diuretics a marked reduction in cardiac toxicity may be obtained without impairment of their diuretic efficiency.

G. B. West

CHEMOTHERAPY

2261. **Studies in Tuberculosis Chemotherapy. I. Simple Primary Aromatic Amines, *in vitro* and *in vivo***

L. DOUB and G. P. YOUMANS. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **61**, 407–421, March, 1950. 16 refs.

Previous work by Kuroya and others showing that the derivatives of primary aromatic amines, such as anilines, are highly tuberculostatic *in vitro* was confirmed. Many of the compounds were inactivated by serum to a considerable degree. This, and the high toxicity, may account for the failure of all of them to exert a definite suppressive effect on experimental mouse tuberculosis.

P. D'Arcy Hart

2262. **The Chemotherapeutic Action of Phenanthridine Compounds. Part I. *Trypanosoma congolense* and *Trypanosoma rhodesiense***

G. BROWNLEE, M. D. GOSS, L. G. GOODWIN, M. WOODBINE, and L. P. WALLS. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 261–276, June, 1950. 28 refs.

As a result of the considerable interest aroused by the introduction of dimidium bromide (2 : 7-diamino-9 phenyl-10-methylphenanthridinium bromide) in the treatment of African bovine trypanosomiasis caused by *T. congolense* and *T. vivax*, a careful and systematic survey was made of a series of phenanthridinium compounds for trypanocidal activity. The antibacterial activity of these compounds was also examined. It had previously been shown that high trypanocidal activity is a property of quaternary salts containing a primary amino group in the 7- and a phenyl group in the 9-position. The activity is also enhanced by the presence of a second primary amino group.

The present work was designed to test these conclusions further and it was confirmed that high activity is present in 9-phenylphenanthridinium salts with two primary amino groups, one of which must be present in the phenanthridine ring. The 2-amino- were more effective than the 7-amino- compounds against both *T. congolense* and *T. rhodesiense*, though it is a characteristic of the series that they are much more effective against *T. congolense*. The compound 2 : 7-diamino-*p*-aminophenyl-10-methylphenanthridinium chloride (" 150 C 47 ") was the most effective compound in the series for the treatment of *T. congolense* and *T. rhodesiense* infections in mice. Against *T. rhodesiense* it was about as active as pentamidine isethionate, but did not possess the same prophylactic properties.

The 6-amino- compounds were also highly effective, but the 8-amino- compounds were comparatively inactive. Compounds of the 2 : 7-diamino- type, but with other substituents in the 9-position such as *p*-nitrophenyl, 2-thienyl, and benzyl, were also highly active against *T. congolense*, but the 9-benzoyl compound was much less effective. The high activity of the triamino-compound (150 C 47), which is about one and a half times as active as dimidium against *T. congolense*, results from a progressive increase in trypanocidal activity as the basic 9-phenylphenanthridinium system is substituted with amino groups. If the primary amino groups were modified by acetylation or other means the trypanocidal activity was considerably reduced. Alkoxy compounds, such as 7-alkoxy-9-*p*-aminophenylphenanthridinium, were also effective against *T. congolense*, even when a nitro group was substituted for the amino group.

The phenanthridinium compounds were found to kill both Gram-positive and Gram-negative organisms, but their antibacterial properties were not closely related to their trypanocidal potencies. In the antibacterial tests a potent antagonist was desoxyribose nucleic acid.

It is suggested that trypanocidal activity may be dependent to some extent on the oxidation-reduction properties of the quaternary salts. *R. Wien*

2263. **The Chemotherapeutic Action of Phenanthridine Compounds. Part II. *Trypanosoma cruzi***
L. G. Goodwin, M. D. Goss, J. A. Lock, and L. P. Walls. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 277–286, June, 1950. 19 refs.

Chagas's disease, caused by *Trypanosoma cruzi*, is much more resistant to chemotherapy than are other trypanosome infections; it is therefore interesting to note that the authors describe experimental evidence of the efficacy of two phenanthridinium compounds which show some promise for the treatment of this South American disease. The two compounds are " 3 C 47 " (2 - amino - 9 - *p* - carbethoxyaminophenyl - 10 - methyl - phenanthridinium bromide) and " 74 C 48 " (3-amino-9 - *p* - carbethoxyaminophenyl - 10 - methylphenanthridinium ethanesulphonate).

Of over 200 compounds examined, 18 showed marked suppressive action, and all but one of these were 9-phenylphenanthridinium salts. A urethane group was contained in 11 of the compounds. There appears to be no satisfactory explanation of the significance of the urethane group in activity against *T, cruzi*. The compounds were tested against *T. cruzi* infections in mice, and the tests were carried out in two ways, by giving the drug during the incubation period of the disease, and by studying the effect of the drug on established infection. The results in established infection were disappointing compared with those obtained during the incubation period of the disease.

There was little relation between the effects of the phenanthridinium compounds on *T. cruzi* and on *T. congolense*. Though activity against *T. cruzi* in the incubation period of mouse infections was generally demonstrated for 9-phenylphenanthridinium salts containing both a urethane and an amino group, no generalization could be made for bisurethane salts. Only two compounds had much effect on established infections, namely, the 2-amino-9-*p*-urethanophenyl compound, " 3 C 47 ", and the 3 : 4′-diurethano-compound " 494 C 46 ". Since the preparation of " 3 C 47 " involved a large number of steps, it was desirable to find a more accessible drug, and the analogue " 74 C 48 " proved to be as active in established infections and markedly less toxic.

The compounds were given by subcutaneous injection daily for 4 to 10 days. The criterion of activity was the presence or absence of trypanosomes in the peripheral blood of the mice for one to two weeks after the last dose of the drug. [By this assessment even the two compounds 3 C 47 and 74 C 48, which showed a high order of activity, might not necessarily produce a permanent cure; it remains to be seen whether these compounds will fulfil clinically the promise they show in experimental infections.] *R. Wien*

2264. **The Chemotherapeutic Action of Phenanthridine Compounds. Part III. The Pharmacological Properties of 3 - Amino - 9 - p - carbethoxy - aminophenyl - 10-methyl-phenanthridinium Salts**
L. G. Goodwin, M. D. Goss, and J. A. Lock. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 287–305, June, 1950. 8 figs., 7 refs.

The compound 3-amino-9-*p*-carbethoxyaminophenyl-10 - methylphenanthridinium ethanesulphonate, or " carbidium ethanesulphonate ", was the most active of the phenanthridinium compounds tested against *Trypanosoma cruzi* infections in mice, and accordingly its pharmacological properties were examined in detail with a view to treatment of Chagas's disease in man. The trypanocidal activity was also examined in more detail. Though some mice were cured of trypanosome infection as judged by the examination of smears and by sub-inoculation into other animals, others continue to harbour occasional parasites in the peripheral blood, though they remain alive long after the control animals have died. The drug may nevertheless be of use in the acute stage of the disease in man.

The drug is only effective given parenterally. It causes necrosis if injected subcutaneously or intramuscularly, but is well tolerated intravenously. The average lethal doses for intravenous and subcutaneous injections in mice were 10 and 130 mg. per kg. respectively. Chronic toxicity experiments were carried out on mice and rabbits. In mice, subcutaneous injection caused local irritation, and in rabbits there was no alteration in the blood picture after the administration of ten doses of 7·5 mg. per kg. intravenously during a period of 14 days. The blood urea level rose during the administration of the compound, but there was no albuminuria. The drug was concentrated in the liver and kidneys and excreted principally in the bile. Though no permanent damage to liver or kidney was observed, the possibility of renal damage must be borne in mind when phenanthridinium compounds are used in man.

The compound was administered both intramuscularly and intravenously in man. In the former case 2 ml. of 0·5% solution was injected into the right deltoid muscle,

and in the latter case 8 ml. was injected intravenously. After intramuscular injection there was a slight swelling of the arm which disappeared on the second day, leaving only a slight tenderness which persisted for 2 to 3 weeks. After intravenous injection the blood pressure fell slightly, and the pulse rate rose for 5 minutes. A bitter taste was perceptible, lasting for 2 hours. There was flushing and a feeling of warmth in the face, persisting for 3½ hours.

Absorption and excretion studies were carried out, the compound being estimated by diazotization of the primary aromatic amino group in the 3-position, and coupling with N-naphthylethylenediamine to produce an azo-compound which is pinkish-purple in colour and can be estimated colorimetrically. After intravenous injection into rabbits the drug appeared in the bile within a few minutes, and the excretion rate increased to a maximum within one hour after injection. After 4 to 5 hours about one-quarter of the dose had been recovered from the bile. The fate of the drug could also be followed visually, since it fluoresces a bright orange colour in ultraviolet light. At about the same time as the drug was detected in the bile the kidneys also began to fluoresce. The fluorescence was confined to the cortex of the kidney. In cats, intravenous injection of the drug caused a transient fall in blood pressure and depression of respiration. Kidney volume slightly increased and then decreased. Blood flow through the kidneys was slower during the fall in blood pressure, and there was a compensatory rise in the rate of flow coinciding with the recovery of the blood pressure. There was no apparent action on the central nervous system, as judged by experiments on the knee-jerk in cats.

R. Wien

2265. **The Mode of Action of Hetrazan on Filarial Worms**
F. HAWKING, P. SEWELL, and J. P. THURSTON. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 217–238, June, 1950. 6 figs., 9 refs.

This paper is a detailed account of the investigations underlying the authors' preliminary communication (*Lancet*, 1948, **2**, 730) on " hetrazan " (1-diethylcarbamyl-4-methyl-piperazine).

The action of hetrazan against all stages of the filarial worm *Litomosoides carinii* in the cotton rat was studied. Hetrazan, or serum from an animal treated with hetrazan, had no action against microfilariae *in vitro*. *In vivo*, a dose of hetrazan caused the microfilariae to disappear rapidly from the circulation and to collect in the sinusoids of the liver, where they were destroyed by phagocytes. Normally the presence of the worms stimulates no cellular response, and it is suggested that hetrazan acts in a similar manner to that of an opsonin upon bacteria, or of suramin upon trypanosomes. A small number of microfilariae were destroyed by the spleen.

The distribution of microfilariae in the capillaries of the tissues was estimated by counting them in measured areas of histological sections; before a dose of hetrazan 63% were in the blood, 30% in the lung capillaries, and 2·6% each in the liver and kidneys. After a dose of hetrazan only 20% remained in the circulating blood, 4% were in the lungs, and 75% in the liver.

No action was observed upon microfilariae in the pleural cavity, and the blood stream was replenished from this source. Hetrazan had no effect upon the rate at which microfilariae migrated towards the anode in cataphoresis experiments. No significant inhibition of the action of hetrazan *in vivo* was observed in animals previously treated with compounds of similar chemical structure (diethylurea, nicotinamide, nicotinic acid, nikethamide, quinine, " miracil D "). Hetrazan had only a very slight effect upon adult worms, even in animals treated for 108 days with the drug; no action was observed upon adult worms *in vitro*.

A small number of experiments with cotton rats protected with hetrazan indicated that the drug killed the larvae of *L. carinii* at the time when they invaded from the mite vector, but there was much less action upon immature worms which had been allowed to establish themselves for a day or two. Hetrazan had no effect on the development in mosquitoes of *Dirofilaria repens*, a filarial worm of the dog. *L. G. Goodwin*

2266. **Chemotherapy of Experimental Filariasis**
P. SEWELL and F. HAWKING. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 239–260, June, 1950. 15 refs.

In a previous paper the authors have described a method of maintaining cyclical transmission of the filarial worm *Litomosoides carinii* in the cotton rat. About 2,500 laboratory-infected rats have now been used in a survey of the therapeutic effect of a wide selection of chemical compounds.

A rough preliminary toxicity test was made with each substance upon groups of 2 mice, doses being given intraperitoneally every day for 4 days. About half of the maximum tolerated dose per kg. for mice was then injected daily for 6 days into cotton rats which had been exposed to infection with *L. carinii* 9 weeks previously, and which showed microfilariae in the peripheral blood.

The cotton rats were killed 5 to 7 days after the end of treatment and the adult worms in the pleural cavities examined, counted, and tested for viability by exposure to bright light in saline at 37° C. The pleural exudate was examined for microfilariae.

Male worms were found to be more resistant and more variable in response to active drugs than were female worms; the efficiency of treatment was therefore judged by the numbers of female worms killed. The therapeutic index of an active drug was estimated from the ratio of the maximum tolerated dose to the minimum dose which killed more than half of the female worms.

The compounds examined included antimonials, arsenicals, arsenic-antimonials, amidines, *iso*thioureas, amidoxines, diguanides, sulphones, sulphonamides, hydroxylamine derivatives, hydroxamic acids, pyridines, substances related to hetrazan, pyrimidines, quinolines, styrylquinolines, anilquinolines, *iso*quinolines, cyanines, phenanthridinium compounds, acridines, benzthiazoles, benziminazoles, benzoxazoles, tetrazoles, thiazolines, xanthones and thioxanthones, benzepines, and miscellaneous dyes and other substances.

All of the antimonials tested except tartar emetic were active, and " pentostam " (sodium stibogluconate),

methyl glucamine stibonate, and "Sdt 779" (4-carbamino-3-(bisdioxypropyl)aminophenyl antimony dipyrocatechinate tetra-sodium disulphite) were outstanding. Four of the 12 arsenicals studied were active, the best being a derivative of *p*-benzamide arsenoxide, neoarsphenamine, and a tervalent derivative of tryparsamide.

Of 35 styryl- and anil-quinolines 23 showed some activity; two phenanthridinium salts, proguanil, and a cyanine dye were also active.

The only substances to show activity against microfilariae were hetrazan and N : N : N′-trimethyl-N′-diethylcarbamylethylenediamine. [This is a valuable survey upon a standardized laboratory infection, and will serve as a basis for future chemotherapeutic investigations. The detailed effects of the drugs are listed in tables which cover a total of 220 substances.]

L. G. Goodwin

2267. **Comparison of the *in vitro* Activity of "Nisulfazole" with That of Other Sulfonamides**
M. C. COLGLAZIER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **35**, 875–884, June, 1950. 4 figs., 17 refs.

"Nisulfazole" is 2-(*p*-nitrobenzenesulphonamido)-thiazole and has been of use in treating intestinal infections, including ulcerative colitis. Its bactericidal activity *in vitro* was compared with that of sulphapyridine, "nisulfadine", sulphaguanidine, "sulphathalidine", and succinylsulphathiazole. *In vitro*, nisulfazole was more active than all these compounds against *Bacterium coli*, *Salmonella paratyphi*, A and B, *Salmonella enteritidis*, *Shigella dysenteriae* Shiga and Flexner, and *Streptococcus viridans*. It was less active than other sulphonamides against *Staphylococcus albus*, *Brucella abortus*, *Salmonella typhi*, and *Bacillus oedematicus* although nisulfazole is partly reduced to sulphathiazole. The fact that it is in many cases superior to sulphathiazole suggests that the nitro compound itself, or some other intermediate reduction product, is active *in vitro*.

G. M. Findlay

ANTIBIOTICS

2268. **A Menispermacea from Japan: *Stephania cepharanthia* Hayata and its Bacteriostatic Action on the Tubercle Bacillus.** (Sur une ménispermacée du Japon: le *Stephania cepharanthia* Hayata et sur son activité bactériostatique vis-à-vis du bacille de Koch)
R. PARIS and A. GERMAN. *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences* [*C.R. Acad. Sci., Paris*] **230**, 2345–2347, June 26, 1950. 2 refs.

Claims have been made in Japan that the roots of *Stephania cepharanthia* are of use in the treatment of tuberculosis, leprosy, and whooping-cough. This action is said to be associated with cepharanthine, one of the four alkaloids present in the root. According to the present authors both the powdered root and cepharanthine acetate have a bacteriostatic action on a human strain of tubercle bacillus. The alkaloid is inhibitory in a dilution of 1 in 50,000. Toxicity for animals is very low: a dose of 1·25 g. per kg. when given subcutaneously kills all mice whereas the LD 50 for mice by the same route is 1·0 g. per kg. body weight. *G. M. Findlay*

2269. **Antibiotic Spectrum of *Hemophilus pertussis***
E. B. WELLS, C. SHIH-MAN, G. G. JACKSON, and M. FINLAND. *Journal of Pediatrics* [*J. Pediat.*] **36**, 752–757, June, 1950. 4 refs.

The results of *in vitro* tests for sensitivity of recently isolated strains of *Hemophilus pertussis* to nine antibiotics were presented. The most active of these, on a weight basis and under the conditions of these tests, were polymyxin (polymyxin D) and aerosporin (polymyxin B). and both of these agents were about equally active, Chloromycetin, aureomycin, and terramycin ranked next in effectiveness and these three agents also had essentially equal activity. Penicillin was about as active as the three latter agents, but streptomycin and neomycin were appreciably less active. Bacitracin was the least effective in these tests. Some of the difficulties of interpreting these *in vitro* findings were discussed, particularly with respect to their therapeutic implications.—[Authors' summary.]

2270. **The Action *in vitro* of Penicillin, Streptomycin, Aureomycin, and Chloramphenicol on Viruses of the Lymphogranuloma–Psittacosis Group.** (Action *in vitro* de la pénicilline, de la streptomycine, de l'auréomycine et de la chloromycétine sur les virus du groupe lymphogranulomatose-psittacose)
G. BARSKI and J. MAURIN. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **78**, 759–764, June, 1950. 17 refs.

Penicillin, streptomycin, and aureomycin in concentrations of 10 to 100 μg. per ml. cause no loss of pathogenicity in the viruses of lymphogranuloma venereum and psittacosis after exposure for 2½ to 3 hours *in vitro* at room temperature. Under the same conditions chloramphenicol causes very slight attenuation in psittacosis virus, but none in lymphogranuloma venereum virus. At 37° C. chloramphenicol (50 μg. per ml.) increases the rate of destruction of lymphogranuloma venereum virus, although at the end of 24 hours the virus is still active. *G. M. Findlay*

2271. ***In vitro* Activity, Absorption and Excretion of Chloromycetin**
G. TUNEVALL and A. R. FRISK. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **2**, 162–167, 1950. 2 figs., 8 refs.

Using 0·05 ml. of a 10^{-3} dilution of 18-hour cultures as inocula, the authors compared the effects of chloramphenicol (in brain-heart infusion) *in vitro* with those of aureomycin (in thioglycollate broth). Chloramphenicol was assayed in the brain-heart infusion medium, with a strain of *Klebsiella pneumoniae* (sensitive to 0·4 μg. per ml.) as test organism. With 8 strains of Gram-positive organisms, aureomycin was some 30 to 100 times more active and with 8 strains of Gram-negative organisms (except for *Proteus vulgaris*) some 5 times more active than chloramphenicol.

Single oral doses of 1 g. chloramphenicol gave maximum levels in blood in 1 hour (10 μg. per ml.) and the antibiotic had disappeared in 24 hours. With 1 g. 8-hourly, a mean level of 4 to 10 μg. per ml. in blood was attained. Urinary excretion was also very rapid, 80% being excreted in 4 hours, and excretion was complete in 8 to 12 hours. Conjugation starts rapidly and the antibiotic is largely excreted in the urine in the inactive form. Thus chloramphenicol is absorbed and excreted more rapidly than aureomycin, and the optimum interval between oral doses is 4 hours.

Malcolm Woodbine

2272. **The Action of Synthetic Chloramphenicol on the Typhoid Bacillus Studied by Means of the Phase-contrast Microscope.** (Action du chloramphénicol synthétique (tifomycine) sur le bacille typhique *Eberthella typhosa* étudiée au moyen du microscope à contraste de phase)
C. LEVADITI, A. VAISMAN, and J. HENRY-EVENO. *Presse Médicale* [*Pr. méd.*] **38**, 665–666, June 14, 1950. 4 figs., 4 refs.

Pour plates were made with inocula of *Salmonella typhi*, and one hour later a drop of synthetic chloramphenicol solution (10,000 units per ml.) was placed on the surface of the medium. At various intervals afterwards organisms were picked from the zone immediately around the drop where complete lysis was seen, from the zone around the outer edge of the first, and from further out. These organisms were examined in fresh preparations by phase-contrast microscopy. Morphological changes were seen which varied directly in severity with the proximity of the organism to the antibiotic and duration of exposure. In general they consisted of changes in size and shape, followed by the appearance of cytoplasmic granules, and eventually complete lysis.

Similar experiments with penicillin instead of chloramphenicol gave qualitatively similar results, but the changes were more rapidly induced and were more marked than was the case with chloramphenicol.

In a series of mice inoculated with cultures of typhoid bacilli and receiving chloramphenicol by mouth the same changes were seen in organisms obtained from the peritoneal exudate 1 to 2 hours after inoculation, together with an intense phagocytosis by polymorphonuclear leucocytes and large monocytes. The authors believe both bacterial changes and leucocytic activity to represent specific effects of the treatment of the infection with chloramphenicol. *E. A. Brown*

2273. **Biochemical Observations on the Mode of Action of Polymyxin.** (Recherches biochimiques sur le mode d'action de la polymyxine)
C. LATTERRADE and M. MACHEBOEUF. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **78**, 753–758, June, 1950. 3 figs., 10 refs.

Polymyxin B, like streptomycin, is a strongly basic polypeptide which forms insoluble compounds in water, in the absence of electrolytes with ribose nucleic acids, phospho-aminolipids, heparin, and bile acids. In addition, polymyxin forms precipitates with mononucleotides. Neutral salts, even when present in a feeble concentration, prevent the formation of these precipitates. As a result of this power of combination polymyxin, like streptomycin, can agglutinate bacteria which are lacking in O-antigen, on condition that the medium is poor in electrolytes. *G. M. Findlay*

2274. **Isolation of a New Antibiotic Substance " Luteomycin " from a Strain of Streptomyces.** [In English]
T. HATA, T. HIGUCHI, Y. SANO, and K. SAWACHIKA. *Kitasato Archives of Experimental Medicine* [*Kitasato Arch. exp. Med.*] **22**, 229–242, Dec., 1949. 14 refs.

A new antibiotic has been obtained from a strain of *Streptomyces* (No. 144), found in soil near Tokyo. The antibiotic, termed " luteomycin ", is very similar in its bacteriological spectrum to aureomycin. It differs from aureomycin, aureothricin (now known as farcinin), and actinomycin A in certain of its physical properties. It is five times more toxic than aureomycin. Serum causes some loss of bacteriostatic activity.

G. M. Findlay

2275. **The Pharmacology of Terramycin**
S. Y. P'AN, J. C. REILLY, T. V. HALLEY, G. H. RICHARD, A. M. PEKICH, and H. A. POLLETS. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **99**, 234–244, June, 1950. 4 figs., 5 refs.

The pharmacology of terramycin has been studied in mice, rats, cats, and dogs. In addition to partially purified and crystalline terramycin, the hydrochloride, the sulphate, and two forms of the sodium salt of terramycin (*p*H 8·5 and 9·5) were available. Toxicity for animals is low: the intravenous LD 50 of the hydrochloride for mice and rats is 192 and 280 mg. per kg. respectively. Sodium terramycin has a similar toxicity in mice. By mouth and subcutaneously the LD 50 of the hydrochloride is 7,200 and 829 mg. per kg. respectively and for sodium terramycin 4,410 and 270 mg. per kg. respectively. Daily intramuscular injections of 40 mg. of sodium terramycin per kg. were tolerated by 2 dogs for more than 60 days, and after periods of 47 to 57 days dogs were not incapacitated by daily oral doses of 80 to 400 mg. per kg. Two dogs given daily intramuscular injections of 160 and 240 mg. per kg. of sodium terramycin died in 6 and 18 days respectively, with cloudy swelling and fatty changes in the convoluted tubules of the kidney.

Daily administration of 80 to 160 mg. per kg. of sodium terramycin for 6 to 7 weeks did not affect the normal growth rate of rats or mice. When given intramuscularly or subcutaneously aqueous solutions of terramycin hydrochloride or sodium terramycin gave rise to irritation, and intravenous injection of a 5% solution of either preparation sometimes caused phlebitis. Slow intravenous injection of a single dose of 100 mg. per kg. of either sodium terramycin or terramycin hydrochloride caused no change in the blood pressure of anaesthetized cats and dogs.

The authors, in a footnote, state that the bioassay of all terramycin preparations employed in these experiments was based on a dihydrate of amphoteric terramycin which

had been assigned an activity of 1,000 μg. per mg. Since then a new standard terramycin has come into use: the old standard has an activity of 925 μg. per mg. when assayed against the new master standard. All dosages given in this paper should therefore be reduced by 7% to conform to the new standard. *G. M. Findlay*

2276. **Prolongation of Therapeutic Levels of Penicillin in Blood by Implantation of Procaine–Penicillin Tablets.** (Prolongacion de la penicilinemia por medio de implantes de tabletas de procaina penicilina)
F. Huidobro, R. Croxatto, and A. Lucchini. *Revista Médica de Chile* [*Rev. med. Chile*] **78**, 363–366, June, 1950. 2 figs., 7 refs.

Subcutaneous or intramuscular implantation of procaine-penicillin tablets prolongs therapeutic blood levels for several days. Tablets consisted of procaine penicillin G with 20% ox fat. Implantation of 400 to 800 mg. tablets gave a detectable level of penicillin in the blood for 14 days, and of a 1 g. tablet for 23 days. The tablets caused no local or general reactions, and the authors discuss their possible uses, especially in preventing post-operative infection and in the treatment of syphilis. *René Méndez*

2277. **Micropowdered Procaine Penicillin by Inhalation**
G. V. Taplin, W. Greene, W. Ralston, W. Adolph, and L. Baurmash. *Annals of Allergy* [*Ann. Allergy*] **8**, 396–403, May–June, 1950. 29 refs.

This investigation was undertaken in order to discover whether procaine-penicillin dust was more or less allergenic than sodium penicillin when inhaled. The particle size varied from below 1 μ to 25 μ, most of the particles having a size of 1 to 2 μ. The incidence of allergic reactions in the 150 patients investigated was 4·6%; this is almost identical with the figure for inhalation of sodium or potassium penicillin micropowders.
H. Herxheimer

2278. **The Effective Concentrations of Penicillin *in vitro* and *in vivo* for Streptococci, Pneumococci, and *Treponema pallidum***
H. Eagle, R. Fleischman, and A. D. Musselman. *Journal of Bacteriology* [*J. Bact.*] **59**, 625–643, May, 1950. 3 figs., 26 refs.

The minimal effective concentration of procaine penicillin in the serum of mice sufficient to abort clinical infection following intramuscular injection of group A streptococci, group B streptococci, and types I and III pneumococci was found to be 0·012, 0·08, 0·08, 0·05, and 0·05 mg. per ml. In mice receiving group B streptococci by intramuscular, subcutaneous, or intratesticular injection and direct injection into the lung, the values were 0·12, 0·1, 0·07, and 0·1 mg. per ml. respectively. In rabbits infected by the intratesticular injection of *Treponema pallidum*, the values varied from 0·005 to 0·01 mg. per ml. Approximately the same values were obtained with aqueous penicillin.

In *in vitro* tests, the levels necessary to kill the same organisms were regularly one-half to one-fifth of those given above. The discrepancy between the *in vivo* and *in vitro* values is accounted for partly by the fact that about half the penicillin in serum is bound to the serum proteins and partly because the concentration of penicillin in the tissues is probably lower than that in the serum. For these reasons, it is probable that the effective concentration of penicillin at the actual focus of infection is of the same order of magnitude as that which obtains *in vitro*.

Thus for the organisms studied, penicillin is effective *in vivo*, so long as its serum concentration is two to five times the minimal bactericidal level as determined by tests with the serum *in vitro*. *R. Hare*

2279. **Histological Reactions to Injections of Procaine Penicillin in Oil**
P. Story. *British Medical Journal* [*Brit. med. J.*] **1**, 1467–1468, June 24, 1950. 3 figs., 9 refs.

2280. **A Study of Streptomycin Excretion in Patients with Renal Insufficiency and Azotaemia.** (Étude de l'élimination de la streptomycine chez des sujets atteints d'insuffisance rénale avec azotémie)
L. Sherman-Warczewski. *Annales de Médecine* [*Ann. Méd.*] **51**, 174–189, 1950. 3 figs., bibliography.

A detailed study was made of blood and urine streptomycin levels following a single intramuscular dose in two groups of patients. The first group consisted of 6 patients with renal disease whose blood urea concentration was higher than 100 g. per 100 ml.; the second group consisted of 6 patients with normal renal function. Urinary excretion of streptomycin was consistently lower and blood concentration higher in the former group over a period of 24 hours. The author holds that these results are sufficiently striking to indicate the need for an assessment of renal function in patients requiring streptomycin therapy, and a suitable modification of dosage where renal impairment is found.
T. A. A. Hunter

2281. **Blood Levels and Urinary Excretion of Aureomycin after Intravenous and Intramuscular Administration**
T. M. Gocke, E. B. Wells, H. S. Collins, and M. Finland. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 100–112, July, 1950. 6 figs., 25 refs.

Previous reports on the absorption and excretion of aureomycin are reviewed and the authors' own investigations described. The concentration of aureomycin in the blood and urine following the administration of 100- and 500-mg. doses intravenously and intramuscularly was determined in groups of 2 or 3 normal subjects, or patients convalescent from minor illnesses who had not been treated with any antibacterial agent. All had normal renal function, and the normal undiluted urine had no antibacterial action. For intravenous injection crystalline aureomycin hydrochloride was dissolved in 5% aqueous solution of dextrose; solutions for intramuscular injection contained leucine buffer and procaine in addition. Serum and urine concentrations of aureomycin were determined by a modification of the Rammelkamp method for penicillin.

On intravenous administration by continuous drip infusion over ½ to 1 hour, a decreasing concentration of aureomycin was detectable in the serum for 12 hours after a 500-mg. dose and for 2 to 4 hours after a 100-mg. dose. No aureomycin could be detected in the blood after similar doses given intramuscularly. On intravenous injection the most rapid rate of excretion in the urine occurred within 8 to 12 hours after a 500-mg. dose, but when the same dose, which was highly irritating, was given intramuscularly it was excreted irregularly. A 100-mg. dose given intramuscularly was excreted rapidly during the first 3 hours. Appreciable amounts of aureomycin were excreted for 2 to 4 days after intravenous injection, and for 8 days after intramuscular injection. After intravenous injection 26 to 50% of the dose was recovered from the urine as active aureomycin, whereas 13 to 24% was recovered after intramuscular injection. In view of the rapid deterioration of aureomycin in neutral or alkaline solution, and particularly in view of reports that aureomycin is protected from deterioration in tissues, it is concluded that much of the loss of antibiotic occurred during manipulation of the samples. The marked irritation caused by intramuscular injection of aureomycin tends to keep the agent localized at the site of injection, and the intravenous route is therefore preferable. Rough estimations indicate that aureomycin is cleared from the plasma at the rate of 40 to 70 ml. of plasma per minute, which is similar to the clearance rate for streptomycin. It is concluded that aureomycin is excreted by glomerular filtration alone.

P. B. Marshall

2282. **The Experimental Background and Clinical Use of Antibiotics**

P. H. LONG, E. A. BLISS, E. B. SCHOENBACH, C. A. CHANDLER, and M. S. BRYER. *Lancet* [*Lancet*] **1**, 1139–1145, June 24, 1950. 1 ref.

See also Sections Dermatology, Abstract 2523; Infectious Diseases, Abstracts, 2593; 2600, and 2614.

TOXICOLOGY

2283. **Acceleration of Carbon Monoxide Elimination in Man by High Pressure Oxygen**

N. PACE, E. STRAJMAN, and E. L. WALKER. *Science* [*Science*] **111**, 652–654, June 16, 1950. 1 fig., 12 refs.

After exposure to carbon monoxide 10 normal subjects were made to breathe pure oxygen under approximately 2·5 atmospheres pressure. Blood samples were taken at 15-minute intervals and analysed for CO by the method of Scholander and Roughton (*J. biol. Chem.*, 1943, **148**, 551). The rate of CO elimination was greatly increased by the high pressure of oxygen. Women lost CO about 30% more rapidly than did men. At 2·5 atmospheres pressure the amount of oxygen in physical solution in the blood was of the order of 4·5 vol. per 100 ml.; thus the normal resting arterio-venous oxygen difference can be covered entirely by the oxygen physically dissolved. High-pressure oxygen breathing will thus also relieve the hypoxic condition in patients suffering from carbon-monoxide poisoning. *A. Schweitzer*

2284. **Effect of Iron Preparations on "Antabuse"-Alcohol Toxicosis**

E. JOKIVARTIO. *Quarterly Journal of Studies on Alcohol* [*Quart. J. stud. Alcohol*] **11**, 183–189, June, 1950. 9 refs.

Intravenous injection of 45·6 mg. of ferrous chloride with ascorbic acid abolished immediately the toxic symptoms caused by taking alcohol after "antabus" and postponed their appearance if the injection was given before the alcohol was taken. It is suggested that antabus poisons the alcohol-oxidizing enzyme and that, since antabus forms an insoluble compound with iron, this poisoning action is prevented by iron and the enzyme system is able to act normally. *V. J. Woolley*

2285. **The Treatment of Acute Alcoholic States with ACTH and Adrenocortical Hormones**

J. J. SMITH. *Quarterly Journal of Studies on Alcohol* [*Quart. J. Stud. Alcohol*] **11**, 190–198, June, 1950. 1 ref.

Patients with acute alcoholic poisoning were treated with adrenocorticotrophin (ACTH) or adrenal cortical extract (ACE), the latter being sometimes supplemented with deoxycortone. Two patients suffering from Korsakoff's psychosis were greatly benefited by ACE and not improved by ACTH treatment. Of 80 patients with acute intoxication ACE was given to 70 and ACTH to 10. ACE had a more rapid sedative action and abolished anorexia sooner, but the differences were slight. Of 66 patients with delirium tremens ACTH was given to 6 and proved greatly superior in effect to ACE, which was given to the remaining 60. *V. J. Woolley*

2286. **Fatal Hepatorenal Syndrome Associated with Phenurone Therapy**

R. W. LEVY, D. J. SIMONS, and S. ARONSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **242**, 933–936, June 15, 1950. 2 figs.

A man, aged 32, had been under treatment with 0·5 g. phenytoin daily for epilepsy. In spite of this, he still had an attack about every 3 or 4 months. He was admitted to hospital in June, 1949, and thoroughly examined. The blood picture, the urine, and radiographs of skull and chest all appeared normal. The electroencephalogram and pneumo-encephalograms were consistent with a diagnosis of epilepsy and slight ventricular dilatation. He was given 1·0 g. of "phenurone" (phenylacetylurea) daily in addition to 0·5 g. of phenytoin a day. After a week, the dose of the former was raised to 1·5 g. a day. In the middle of September he was found to be taking his drugs regularly and with no complications. Ten days later he had a major convulsive seizure, which lasted for 2½ hours and was terminated by intravenous administration of sodium phenobarbitone. After 2 days in hospital, where he was said to have improved somewhat, he was transferred in a semi-stupor to the authors' care. He was found to have a left-sided hemiplegia with normal optic disks. The temperature was raised and the blood pressure was 170/110 mm. Hg, as against 126/74 in June. A few days later he had albuminuria and appeared jaundiced. The blood urea level was high, and the icteric index 42. In spite of treatment he died 10 days later. At necropsy no gross lesions were found, the

liver and kidneys being within normal limits for weight. Histological examination, however, revealed marked hepatitis and severe lower nephron degeneration.

The authors conclude that the most likely cause of death was phenurone intoxication, as it is improbable that phenytoin which had been taken for 9 years would cause a fulminating toxic hepatitis and nephritis. They give a brief description of a case of acute yellow atrophy of the liver, after administration of 51 g. of phenurone over 44 days. They also mention [with no references] 3 other deaths associated with phenurone, one from hepatitis and 2 from aplastic anaemia. Thus in 3 out of 5 deaths associated with phenurone therapy severe liver damage has been a feature.

Reginald St. A. Heathcote

2287. **Treatment of $\beta:\beta'$-Dichlorodiethylsulphide Injuries by Electrophoresis with Cysteine Hydrochloride** (Die Behandlung von $\beta:\beta'$-Dichlordiäthylsulfidverletzungen durch Elektrophorese mit Cysteinhydrochlorid) H. H. MEYER-DÖRING. *Archiv für Experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **209**, 443–455, 1950. 6 figs., 12 refs.

Mustard gas ($\beta:\beta'$-dichlorodiethylsulphide) reacts with cysteine *in vitro* and is destroyed during the reaction. An attempt was made to apply this reaction to the prevention of mustard-gas burns after the application of the toxic agent to small areas of the skin of the forearm. In experiments on 6 volunteers mustard gas in quantities up to 11 mg. was applied to a small area of skin and the cysteine introduced into the tissue by electrophoresis. The anode was the active electrode and electrophoresis was carried out for 20 to 30 minutes at a current strength ranging between 0·1 and 10 mA between platinum or silver electrodes 6 sq. cm. in area and 1·5 to 2·0 cm. apart. Formation of blisters was prevented by this means even when the application of cysteine was not begun until 8½ hours after exposure to mustard gas.

Vera N. Warren

INDUSTRIAL TOXICOLOGY

2288. **Acute Toxicity of Zirconium, Columbium, Strontium, Lanthanum, Cesium, Tantalum, and Yttrium** K. W. COCHRAN, J. DOULL, M. MAZUR, and K. P. DUBOIS. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **1**, 637–650, June, 1950. 29 refs.

The acute oral LD 50 values for five zirconium salts ranged from 990 to 2,290 mg. of zirconium per kilogram; large oral doses of zirconium compounds can, therefore, be ingested without harmful effects. The intraperitoneal LD 50 values ranged from 63 to 939 mg. of zirconium per kilogram, with zirconium sulfate being the most toxic and sodium zirconyl sulfate the least toxic.

Lanthanum compounds exhibited a low toxicity when administered orally. Of six compounds tested, lanthanum ammonium nitrate was the most toxic, the LD 50 being 830 mg. of lanthanum per kilogram. No deaths occurred from doses as high as 10 gm. per kilogram of lanthanum oxide and 5 gm. per kilogram of lanthanum sulfate. When five of these compounds were administered by the intraperitoneal route, the LD 50 values ranged from 134 to 209 mg. of lanthanum per kilogram.

Tantalum oxide was nontoxic when administered orally, while potassium tantalum fluoride, tantalum chloride, and potassium columbate exhibited a low toxicity by this route. When tantalum chloride was given intraperitoneally, the LD 50 was 38 mg. of tantalum per kilogram. Both potassium columbate and columbium chloride were quite toxic to rats when given intraperitoneally, the LD 50 values being, respectively, 86 and 14 mg. of columbium per kilogram.

The intraperitoneal toxicity of five strontium compounds ranged from an LD 50 of 88 to an LD 50 of 247 mg. of strontium per kilogram. Cesium exhibited very low intraperitoneal toxicity to rats except in the case of cesium hydroxide, in which the LD 50 was 89 mg. of cesium per kilogram. Yttrium appeared to be relatively nontoxic; the LD 50 values for three yttrium compounds ranged from 117 to 395 mg. of yttrium per kilogram.

Lanthanum chloride (molar concentration, 1×10^{-5}) was found to be able to replace aluminium as an activator for the succinic dehydrogenase system. Strontium chloride (molar concentration, 4×10^{-4}) was partially effective in replacing calcium in this system. Columbium (5×10^{-4} molar potassium columbate) caused approximately a 50% inhibition and 1×10^{-3} molar yttrium chloride produced a 25% inhibition of the succinic dehydrogenase activity of mouse liver *in vitro*.

Cesium chloride failed to inhibit the adenosine triphosphatase activity of mouse liver *in vitro*, while salts of other metals caused 50% inhibition at the following molar concentrations: columbium chloride, $4\cdot2\times10^{-4}$; potassium columbate, $5\cdot8\times10^{-4}$; lanthanum chloride, $4\cdot4\times10^{-3}$; strontium chloride, $8\cdot3\times10^{-2}$; yttrium chloride $4\cdot5\times10^{-3}$; zirconyl chloride, $1\cdot05\times10^{-3}$.—Authors' summary.]

2289. **Parathion Inhibition of Cholinesterase** H. V. BROWN and A. F. BUSH. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **1**, 633–636, June, 1950. 5 refs.

During an investigation of the effects of exposure to the insecticide, "parathion" (diethyl *p*-nitrophenyl thiophosphate) by the California State Department of Public Health, the authors studied the personnel of a factory manufacturing the material in an attempt to correlate the concentration of parathion in the atmosphere with the cholinesterase activity of blood plasma and erythrocytes. The methods of estimation used are described in detail, and the results are tabulated. Twelve subjects who had intermittent contact with parathion-contaminated air were included in the investigation, but from only 5 of them were successive blood samples obtained. One subject who was not exposed to parathion served as a control.

Air samples showed a maximum concentration of 8 mg. per 10 c.m. and an estimated average exposure of 2 or 3 mg. per 10 c.m. The results of estimation of the cholinesterase activity in blood plasma, although not

compared with an adequate number of control specimens, suggest that there is a decrease during exposure and a pronounced increase within 5 months of removal from exposure. The estimation of cholinesterase activity of erythrocytes in the same group of people gave results which were not nearly so convincing. The authors conclude, however, that continuous exposure to parathion-contaminated air in concentrations of 2 to 8 mg. per c.m. is potentially dangerous. *A. Lloyd Potter*

2290. **Prolonged Inhalation of Cadmium**
F. PRINCI and E. F. GEEVER. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **1**, 651–661, June, 1950. 11 refs.

The effects on dogs of the intermittent inhalation over long periods of cadmium oxide and cadmium sulphide were studied. Ten dogs were exposed to an average concentration of 4 mg. per c.m. of cadmium sulphide, and 10 to the same concentration of cadmium oxide, for 6 hours a day on 5 days a week. Of the particles in the air in the exposure chambers 98% were less than 3μ in diameter. Ten control animals were exposed to air which passed through the chamber at the same lineal velocity (10·5 m. per minute) as that in the exposure chambers. The average total exposure to the sulphide was 895 hours, and to the oxide 1,102 hours. During the period of exposure a variety of estimations were carried out on blood and urine, and finally the dogs were killed and subjected to necropsy. No significant abnormalities were discovered which might indicate serious injury due to the cadmium compounds. While most of the cadmium dust was found to be stored in the lungs, liver, and kidneys, no associated pathological change was found in these organs. No evidence of damage accompanied cadmium levels as high as 0·22 mg. per 100 ml. in the blood, and 0·357 mg. per litre in the urine.

In view of their findings, the authors suggest that the commonly accepted figure for the maximum allowable concentration of cadmium, 0·1 mg. per c.m., is lower than is necessary, and that this might well be raised to 1 mg. per c.m. without producing deleterious effects. They point out, however, that the compounds of cadmium vary considerably in solubility and absorbability, and suggest that the allowable concentration should differ for different compounds and for different physical states of the same compound. *A. Lloyd Potter*

2291. **Toxicity of Cadmium Sulfide and Cadmium Sulfoselenide Pigments**
J. L. GABBY. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **1**, 677–684, June, 1950. 4 refs.

Experiments are described in which the toxicity to piebald rats of cadmium-sulphide and cadmium-sulphoselenide pigments, given by mouth, was determined. These pigments are used in the manufacture of paints and coloured chalks, and are therefore a potential toxic hazard to children. The author found that no adverse symptoms developed in the experimental animals ingesting cadmium-sulphide pigments, and the amount of this pigment introduced into the food seemed to make little difference to them. When the pigment containing selenium was ingested in proportions greater than 1% of the diet it was noticed that a depression of appetite resulted, but this could be attributed to taste aversion as it did not decrease the efficiency of utilization of the food consumed. The conclusion is drawn that no danger exists for children who might ingest paint containing cadmium-sulphide pigment, and that ingestion of chalk containing the cadmium-sulphoselenide pigment might lead to a slight depression of appetite only.
A. Lloyd Potter

2292. **Carbon Tetrachloride Nephrosis. A Frequently Undiagnosed Cause of Death**
R. M. FARRIER and R. H. SMITH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 965–967, July 15, 1950. 1 ref.

Non-industrial poisoning by carbon tetrachloride was the unsuspected cause of nausea, vomiting, diarrhoea, and anuria in 12 patients out of 5,000 admitted to the U.S. Marine Hospital, Staten Island. The drug had either been swallowed or inhaled, but the fumes proved dangerous only in persons under the influence of alcohol. A lower nephron nephrosis with fatal azotaemia developed, unless the patient could be tided over the critical anuric period of about 12 days—the recovery time for the damaged tubular epithelium—by a regimen of restriction of salt-free fluid intake to 800 ml. daily and removal of excess non-protein nitrogen from the blood. Of the various methods recommended, only peritoneal lavage was tried: a fluid containing (in g. per litre) sodium chloride, 6·0; potassium chloride, 0·2; calcium chloride, 0·1; magnesium chloride, 0·1; sodium acid phosphate, 0·05; sodium bicarbonate, 2·0; sodium citrate, 1·57; and dextrose, 20·0, was used in amounts of 30 litres daily. Penicillin, 10 units to each ml., and heparin 1 mg. to each litre, were added. Of the first 12 patients 5 died; of the next 14 " approximately 80% " [presumably 11] recovered. *L. H. Worth*

2293. **Solubility and the Relative Toxicity of Lead Chromate**
G. C. HARROLD and S. F. MEEK. *Industrial Medicine* [*Industr. Med.*] **18**, 407–409, Oct., 1949. 8 refs.

The authors have continued their earlier observations [*J. industr. Hyg.*, 1944, **26**, 47] on 26 men exposed to at least 6·2 mg. per day of lead chromate for over 40 months and for a large part of the time to 15 to 20 mg. per day. At the end of this period the group " basophilic aggregation " (B.A.) was 0·7 and the lead-in-urine average was 0·039 mg. per litre and no abnormal clinical or pathological signs were observed. With lead chromate, unlike lead oxide, there is correlation between the B.A. and lead-in-urine but none with the amounts of lead-in-air. Lead chromate is less readily soluble in human lung fluid than is lead oxide. The authors state that signs of lead absorption will appear more rapidly with the more soluble salts than with the less, and they believe that their work, on the analysis of the amounts of uncoated lead chromate in human pleural fluid, provides an " explanation of the lack of harm due to very large

amounts of inhaled lead chromate ". The amounts of lead chromate found soluble in 1 litre ranged from 1·28 mg. in pleural fluid to 1·14 mg. in serum. Since the amount of tissue fluid acting as an exchange medium between lung and blood is limited, saturation would provide less than 1·0 mg. of lead ion which is subject to continuous unstable equilibrium with the blood and finally the kidney. Maintenance of saturation would require large quantities of lead chromate in the lungs. In the 26 men observed, not only was saturation not reached but the lead-in-urine and the B.A. dropped to normal even when the men were exposed to 6·2 mg. of lead chromate daily. The authors suggest that the lead salts which prove to have solubilities in the range of 1 mg. per litre in human lung fluid are unlikely to cause intoxication from inhalation of less than 20 mg. insoluble lead compound per 10 cubic metres of air.

The authors discuss whether or not levels of urinary excretion higher than that of the general population can be maintained without clinical symptoms. Since the rate in 100 men exposed to large quantities of lead chromate rose to 0·1 mg. per litre with no demonstrable damage, there must be some regulatory mechanism. (The rate in the general population has been reported as 0·05 mg. per litre.) That this rate is in equilibrium with the exposure is shown by the return to normal industrial levels and finally to normal general population levels even though men were exposed to over 6 mg. of lead chromate daily at work. From the results it is concluded that lead intoxication from lead chromate is highly improbable in the industrial exposures likely to be encountered. This conclusion is based almost entirely on the solubility characteristics of this compound. " Where the amounts of lead compounds which can be dissolved in body fluids are equal to, or less than, the amounts which are transported and eliminated without harm, the potential saturation limit is the important factor ". The factor of solubility here is independent of particle size, in contrast with the lead compounds that are more soluble in body fluids. *A. J. Amor*

2294. **Arsine Poisoning. Epidemiologic Studies of an Outbreak following Exposure to Gases from Metallic Dross**
L. W. Spolyar and R. N. Harger. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **1**, 419–436, April, 1950. 2 figs., 21 refs.

THERAPEUTICS

2295. **Mental Changes Occurring in Chronically Anoxemic Patients during Oxygen Therapy**
J. H. Comroe, E. R. Bahnson, and E. O. Coates. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1044–1048, July 22, 1950. 10 refs.

Undesirable effects of oxygen therapy in cases of chronic anoxaemia have been reported several times in recent years. Details are now given of the case of a man with emphysema and congestive heart failure whose cyanosis was relieved by oxygen, but who became stuporose whenever it was administered and ultimately died. Subsequent observations have been made on 65 patients with chronic anoxaemia, 8 of whom showed mental changes varying from somnolence to coma when given pure oxygen; respiratory exchange, blood gas levels, and arterial *p*H were measured in each case. It was found that symptoms may occur if the arterial carbon-dioxide pressure rises above 50 mm. Hg and the oxygen saturation falls below 90%, providing the cyanosis is relieved. The following possible causes are discussed: (1) CO_2 narcosis; (2) cerebral vasospasm: (3) reflex cortical depression; (4) increased pressure of cerebrospinal fluid; and (5) direct depression of the activity of the cerebral cortex by high oxygen tension. No definite conclusion is reached.

In the management of cases of chronic anoxaemia pure oxygen is rarely needed and a 30% concentration seems advisable at first, particular care being taken in the first 3 hours of its administration, when the risk of mental depression is greatest. Once consciousness is lost, respiration is depressed and atelectasis is liable to follow. *K. Gurling*

2296. **Natural and Synthetic Oestrogenic Substances: Their Relative Effectiveness when Administered Orally.** [In English]
Å. B. V. Ryden. *Acta Endocrinologica* [*Acta endocrinol., Kbh.*] **4**, 121–139, 1950. 6 figs., 57 refs.

The therapeutic effects of dienoestrol, oestradiol monobenzoate, and oestrone given orally were compared in 6 surgically castrated mature women. The daily doses given were 3 mg. of dienoestrol, 8 to 10 mg. of oestradiol monobenzoate, and 20 to 24 mg. of oestrone. The effects were noted on the endometrium (by weekly biopsy), subjective symptoms, vaginal mucosa, and size of the uterus as measured by uterine sound. Results were most rapid with dienoestrol; vaginal mucosa was usually restored to normal before disappearance of subjective symptoms. During the first week uterine growth was 1·8 cm. with dienoestrol, 1·4 cm. with oestradiol monobenzoate, and 1·7 cm. with oestrone. This gives an approximate relative potency of 1 to 3·5 to 8. The relative effects on the endometrium were estimated as 1 to 4·5 to 14·5. *C. L. Cope*

2297. **Nine Blood-group Antibodies in a Single Serum after Multiple Transfusions**
J. O. Collins, R. Sanger, F. H. Allen, and R. R. Race. *British Medical Journal* [*Brit. med. J.*] **1**, 1297–1299, June 3, 1950. 4 refs.

A Connecticut woman aged 40 years had two pregnancies, the first ending in toxaemia and premature stillbirth, and the second in normal delivery. At this time splenomegaly was noted, which was said by the patient to have been present for 12 years. No abnormality was found on examination of the blood on three occasions. Four years later splenectomy was performed, the spleen weighing 1,100 g., after which anaemia developed and two blood transfusions were given. During the next 12 years the patient was given a further 18 transfusions for anaemia due to osteosclerosis, and on

four occasions developed a transfusion reaction. On examination of the patient's serum, 9 blood-group antibodies were found, as shown in the following table:

System	Phenotype	Genotype	Antibodies in the Serum
ABO	O	OO	Anti-A and anti-B
MNS	MsMs	MsMs	Anti-N and anti-S
Rh		CDe/cde or CDe/cDe	Anti-E and anti-C^w
Kell	K-	kk	Anti-K
Lewis*	Le(a- b-)	?Le^cLe^c	Anti-Le^a and anti-Le^b
P	P-	pp	—
Lutheran*	Lu(a-)	Lu^bLu^b	—

* See Andresen *et al.*, *Nature*, 1949, **163**, 580.

Of these antibodies, those to E, K, C^w, Le^a and S were probably immune in origin and the remainder naturally occurring. It is surprising that among this wealth of antibodies, five of which are very rare, no anti-P was found, since the patient lacked the antigen P and she must surely have received some P+ blood.

John Murray

2298. **Multiple Antibody Response to Repeated Transfusions**
R. H. MALONE and J. COWEN. *British Medical Journal* [*Brit. med. J.*] **1**, 1299–1300, June 3, 1950.

A woman of 64 received transfusions of blood from 24 donors "compatible" in respect of A, B, O, and D blood antigens, as a result of which she developed antibodies to E, M, and P. The authors state that routine methods of cross-matching are inadequate to detect the rarer antibodies, and that special techniques should be employed in cases of repeated transfusion. They suggest that a search for rare antibodies in the sera of patients who have been repeatedly transfused with so-called compatible blood will reveal that these antibodies are of much more frequent occurrence than is generally believed. *John Murray*

2299. **Dangerous Universal Donors. II. Further Observations on *in vivo* and *in vitro* Behaviour of Isoantibodies of Immune Type Present in Group O Blood**
D. M. ERVIN, R. M. CHRISTIAN, and L. E. YOUNG. *Blood* [*Blood*] **5**, 553–567, June, 1950. 4 figs., 16 refs.

The authors describe the occurrence of severe haemolytic reactions in three group-A (sub-group A_1) individuals on transfusion with group-O whole blood or plasma. In one case 10 ml. of a commercial preparation of soluble A and B factors had been added to 500 ml. of whole blood before transfusion. The anti-A antibodies demonstrated in the donors' serum fixed complement, acted as haemolysins, were difficult to neutralize with soluble A and B factors, and were capable of giving a positive reaction to Coombs's test, while their ability to agglutinate group-A erythrocytes was enhanced by normal human serum. In other words, they had the characteristics of antibodies observed in serum from donors known to have been actively immunized against the A factor by previous transfusion of group-A erythrocytes, by transfusion of A factor, or by pregnancy. A history of such a stimulus was, however, lacking in the case of these donors. Small amounts of immune A antibody were consistently demonstrated in 12 of 100 random samples of group-O serum which, after neutralization, gave indirect positive Coombs tests with A_1 erythrocytes and agglutinated A_1 erythrocytes suspended in compatible normal human serum.

The authors conclude that there is no longer any justification for regarding group-O blood as universally safe for transfusion purposes. They stress that while outward clinical manifestations of a haemolytic reaction may be slight, the laboratory findings may be dramatic. The addition of group-A and group-B substance is not at present sufficient to render all group-O blood safe, and they suggest that all group-O blood should be screened. Many dangerous donors would be eliminated if their serum, diluted 1 in 50, 1 in 100, or 1 in 200 with saline, were tested with a saline suspension of group-A and group-B erythrocytes. If group-O plasma which in such dilution failed to agglutinate erythrocytes of either group were neutralized with soluble A and B factors, some reduction in hazard would be achieved. Tests of neutralized serum against group-A and group-B erythrocytes suspended in the recipient's own serum would serve as an additional precaution in selected cases, especially those receiving multiple transfusions from universal donors. *Janet Vaughan*

2300. **Myocardial Intolerance to Excessive Blood Transfusion**
W. D. HOLDEN, J. W. COLE, and A. F. PORTMANN. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **90**, 455–460, April, 1950. 4 figs.

2301. **The Control of Blood Transfusion Hazards**
R. D. MCCLURE, F. W. HARTMAN, and G. H. MANGUN. *Annals of Surgery* [*Ann. Surg.*] **131**, 628–640, May, 1950. 2 figs., 41 refs.

2302. **Studies on Neuromuscular Dysfunction. XIII: New Concepts and Techniques of Neuromuscular Re-education for Paralysis**
H. KABAT. *Permanente Foundation Medical Bulletin* [*Permanente Fdn med. Bull.*] **8**, 121–143, July, 1950. 12 refs.

This is a further statement of the author's views on the rehabilitation of patients with neuromuscular dysfunction, particularly that due to poliomyelitis.

He emphasizes again that muscular power can be increased by hypertrophy of muscle fibres and that disuse must be prevented; the importance of correct motor patterns is stressed as well as the fact that fatigue in itself is beneficial rather than harmful and that many dormant anterior horn cells can be brought into action by suitable techniques, although they will not respond to maximum voluntary effort. The special techniques include maximal resistance, reflex activity, mass movement patterns, reversal of antagonists, and rhythmic stabilization. [This paper appears to be a simple restatement of the author's views, and to contain nothing beyond what he has recorded in his preceding publications.] *N, S. Alcock*

Medical Jurisprudence

2303. **Compensation in Cases of Hernia of the Intervertebral Disk.** (Considerazioni infortunistiche sull'ernia del disco intervertebrale)
G. BETOCCHI. *Rassegna Medica di Infortunistica e Patologia del Lavoro* [*Rass. med. Infortun. Pat. Lav.*] 3, 241–255, March–April, 1950.

Not more than 800 to 900 operations on intervertebral disks are performed annually in Italy. The author's observations cover about 40 cases, 15 being operated upon. He suggests that current views of this disorder may be unsound and that it is difficult to attribute pain, after chill or acute infection, to mechanical causes. Any malformation of a disk will tend to cause abnormal mechanical stress, falling particularly on adjacent structures, including nerves. By itself the degeneration and distortion of a disk may be painless. From the medico-legal aspect it is important to distinguish between symptoms caused by injury affecting the malformed parts of the spine, and symptoms which would arise from the malformation independent of injury. The cases investigated were mostly in persons engaged in physical work; many persons in sedentary employment, however, suffer from the condition, with no clear history of injury. *G. C. Pether*

2304. **Criminal Abortions Induced by Intrauterine Pastes**
F. R. DUTRA, F. P. CLEVELAND, and H. P. LYLE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 865–869, July 8, 1950. 3 figs., 9 refs.

The injection of pastes into the uterus as a method of inducing therapeutic abortions was introduced in 1931. Many of the patients thus treated developed complications and many deaths have been reported as due to this method. Post-mortem findings have demonstrated the presence of constituents of the paste in the lungs and brain. The basic component of all such pastes is soft soap, combined with small quantities of various aromatic substances. The authors have investigated 4 cases in which death followed attempted criminal abortion by the intrauterine administration of soapy substances. Death resulted in one case from necrosis of the uterine wall with peritonitis, in another from diffuse peritonitis without perforation of the uterus, and in the remaining 2 cases from paste embolism. Soft soap mixed with iodine was responsible for the embolism in one of these last cases, and iodine was found in the heart blood and in the amniotic fluid. The addition of 0·1 ml. of the paste was found to cause immediate haemolysis of 1 ml. of oxalated blood, and in experiments on rabbits the intravenous administration of small doses of the paste proved fatal in a few minutes. A solution of iodine alone produced no effect, but small amounts of the soap were highly toxic. Subcutaneous injection of the abortifacient led to necrosis of the skin, subcutaneous tissue, and subjacent muscle. Two probable reasons why intrauterine pastes are popular with abortionists are the ease with which the paste can be administered, and that complications are unlikely to develop on the premises. The incidence of immediate sudden death appears to be small. That these pastes usually have a strong odour may assist in identification if the case is seen soon after operation. The soaps are irritating, produce tissue necrosis, and cause haemolysis of the blood. Other ingredients may also prove highly toxic. The use of these pastes, even in legitimate practice, is to be condemned. *Gilbert Forbes*

2305. **Attempted Suicide by Poisoning.** (Selvmordsforsok med gift)
G. JOHNSEN and E. VOGT. *Nordisk Medicin* [*Nord. Med.*] **43**, 1013–1017, June 23, 1950. 2 figs., 4 refs.

This is an analysis of all cases of attempted suicide by poisoning admitted to the Oslo Municipal Hospital between 1924 and 1939. There were 278 patients in all (28 having been admitted on two occasions), 124 men and 154 women. Of these 14% died (about 18% of the men and 10% of the women). Age, occupation and social status, causative factors, and the poisons used are analysed. Of all attempts 70% were made with barbiturates, with a mortality of 10%, 15% with alkaloids (mortality 25%), and 13% with inorganic poisons (mortality about 4·5%). *W. G. Harding*

2306. **Some Remarks Concerning the Employment of Narco-analysis in Forensic Psychiatry.** (Einige Bemerkungen zur Frage der forensisch-psychiatrischen Verwendung der Narkoanalyse)
A. SCHÖNKE. *Nervenarzt* [*Nervenarzt*] **21**, 241–244, June 20, 1950. 4 refs.

Is it permissible for a medical expert to administer a suitable anaesthetic to an accused person for purposes of narco-analysis in order to be in a better position to fulfil his task before a court? The legal side of this question is discussed in relation to experience accumulated in Germany, France, and other countries. The author agrees with recent orders given by the Ministers of Justice of two German *Länder* forbidding the application of this method of investigation in penal procedure. In his view administration of a hypnotic drug to the prisoner is not justifiable from the practical, legal, psychological, or moral points of view. *F. F. Kino*

2307. **How to Make Finger-prints Visible in a Third-degree Burn.** (Kenntlichmachung der Papillarlinien bei Verbrennungen III. Grades)
S. SCHÖNBERG. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 334–335, April 1, 1950.

In a case of fatal burning it proved impossible to obtain finger-prints for identification. Both the hands of the cadaver were therefore placed in pure glycerin for 4 weeks and the fingertips were well massaged from time to time. An identifiable finger-print was then obtained.
J. Zeldenrust (*Excerpta Medica*)

Radiology

TECHNIQUE

2308. **Radiography of Cerebral Tumors Employing P^{32}**
D. STEINBERG and B. SELVERSTONE. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 304–308, June, 1950. 3 figs., 6 refs.

When radioactive phosphorus (P^{32}) is given intravenously to patients with brain tumours, the uptake of phosphorus by the tumour tissue can be roughly estimated in biopsy specimens by means of the Geiger–Müller counter to be 5 to 100 times as high as that by normal cerebral tissue, but it is also found that there are marked differences in P^{32} activity between adjacent areas of the same tumour. At the Harvard Medical School and the Massachusetts General Hospital the authors have developed a radioautographic technique which permits of the determination of the P^{32} content in each area of a section of tissue obtained at operation 12 to 72 hours after 0·5 to 4·0 millicuries of P^{32} have been administered intravenously. A frozen-section technique without fixation is employed in order to prevent redistribution of the isotope within the tissues. [For a description the original paper should be consulted.] Radioautography of gross specimens is used to indicate the areas of special interest on which the technique of microradioautography can be concentrated.

The microdensitometric methods employed for estimating the relative radioactivity shown in the various areas of the radioautograph are described. As comparison between cases is made difficult by variations in the dosage and in the time-interval between injection and operation, the uptake of P^{32} in each area is expressed in relation to that of normal cerebral tissue. The results in 18 cases are given, with illustrative plates. The degree of radioautographic blackening from tumour tissue has been consistently found to be higher than that from normal brain tissue, but it varies considerably within the tumour. An increase in radioautographic density is the reflection of increased metabolic activity and rate of phosphorus replacement and not of an increase in total phosphorus content, which appears to be significantly lower in tumours than in normal brain tissue. Examples of the correlation between the microscopical appearances of the radioautograph and of the tissue itself are given.

Edwan M. McGirr

2309. **Percutaneous Angiography of the Vertebral Artery.** [In English]
E. LINDGREN. *Acta Radiologica* [*Acta radiol., Stockh.*] 33, 389–404, May, 1950. 19 figs., 10 refs.

The author briefly reviews techniques previously used for percutaneous cerebral angiography and describes his own. Posterior to the intervertebral canal the cervical transverse process is broad and high, whereas in front of it the bone is narrow and low; the vertebral artery is therefore easily approached from the front. It lies ventro-medial to the nerve roots, but a laterally protruded disk may obscure it without causing symptoms. Percutaneous puncture is therefore best performed fairly high in the neck, the carotid sheath being drawn laterally with the left hand. Puncture too far laterally will cause pain in the shoulder or upper arm, while medially the vertebral body will be struck. If the needle is introduced obliquely and medially it may puncture the theca, and cerebrospinal fluid will force the saline out of the attached glass tube. Often backflow of blood does not follow direct puncture because the artery is transfixed, but slight withdrawal of the needle will correct this. It is essential that a free flow of blood up the glass tube be obtained before contrast medium (35% "umbradil") is injected. Occasionally the vertebral artery is so small that no contrast medium can be introduced.

The author has performed vertebral angiography 60 times with this technique; results were satisfactory in two-thirds of cases. One patient went blind for 3 days and had aphasia for a week, and one was confused for 24 hours. The basilar artery usually runs parallel to the clivus, dividing at or just above the level of the posterior clinoid process, but sometimes it bends backwards for a centimetre; it may also show a slight lateral kink. Minor asymmetries of the superior cerebellar and posterior cerebral arteries, without stretching of the vessels, may also be present in normal subjects. In 0·4% of cases the vertebral artery arises from the carotid and passes directly through the foramen magnum. Interpretation may thus be difficult. In general, pneumography gives more definite information on location of lesions, but angiography is useful where vascular lesions are suspected, or in cases of recurrence of tumour after operation.

John Foley

2310. **Pharmacodynamic Effect of Procaine, Administered Orally, on the Duodenal Bulb.** (La prova farmacodinamica del bulbo duodenale mediante somministrazione per os di procaina)
A. OLIVERI and A. ORANGER. *Radiologia Medica* [*Radiolog. med., Torino*] **36**, 366–375, May, 1950. 6 figs., 24 refs.

In cases in which barium-meal examination showed considerable hypertonus and spastic reaction of the duodenal bulb, the authors administered procaine orally before repeating the examination, and found that this drug has a definite antispasmodic and antikinetic influence on the duodenal bulb. Their experiments proved that in cases of ulcer all indirect signs can be removed by this method, leaving a clear picture of the underlying organic lesion.

The authors administer 1% procaine solution 11 hours, and 2% solution 2 hours, before the examination [dose not given]. They divide their cases into three groups: (1) hypertonic bulb without an organic lesion; (2) hypertonic bulb with ulceration; (3) spastic bulb with cicatricial changes. In group (1) normal filling of the duodenal bulb is secured by this method. In both the remaining groups the signs of ulceration or scarring are definite. *W. J. Czyzewski*

2311. **A Comparative Study of Radiotherapy Techniques**
D. K. SAMBROOK, A. C. THACKRAY, and P. B. WOODYATT. *British Journal of Cancer* [*Brit. J. Cancer*] **4**, 63–76, March, 1950. 10 figs., 6 refs.

It is pointed out that for an accurate comparison to be made of the effects of different radiotherapy techniques only one factor can be varied at a time. In this case fractionation was chosen. Since serial biopsies were needed for the purposes of the experiment, patients with large, accessible tumours, two with basal-cell and five with squamous-cell carcinomata of the skin, and four with carcinomata of the breast, were chosen. Two experimental techniques were used, one giving 500 r twice a week and the other giving 1,000 r once a week. Control was obtained by dividing the tumour into segments, usually halves but sometimes quarters, and treating one of the segments with 200 r given daily.

The technique which gave 500 r showed uniformly good results in 3 cases of epithelioma, no difference being noted between experimental and control areas except possibly in one case, where the advantage was with the experimental technique. In 2 cases of carcinoma of the breast the response in the experimental area was better, and in 2 the response was equal to that in the control area. The 2 cases of basal-cell cancer responded better to the control technique. When 1,000 r was given once a week it produced severe skin reactions in all 4 cases so treated, and in 2 resulted in a necrosis. This technique also failed to control tumour growth in 3 out of the 4 cases.
M. C. Tod

RADIOTHERAPY

2312 (*a*). **End Results of Radiotherapy of Cancer of the Tongue**
J. BAUD. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **63**, 701–711, May, 1950.

The author analyses the results of radiotherapy in 1,055 cases of cancer of the tongue treated at the Curie Foundation, Paris, between 1919 and 1941. The cases are classified in three groups: (*a*) tip and undersurface (86); (*b*) dorsum and edges (638); and (*c*) posterior third (331). They are further grouped according to the extent of the primary growth and (separately) according to extent of secondary spread. The analysis is set out in great detail, and over the long period there has naturally been great diversity of method. For example, nine different methods or combinations of treatment are described for cases in group (*a*) alone. Radium implantation was used alone in 175 cases, and combined with other forms of treatment in 609 cases; external irradiation was used alone in 270 cases with unsatisfactory results. The needles most frequently used for implantation have linear densities of 0·52 and 0·48 mg. per cm. and active lengths of 2·5 and 1·5 cm. respectively. Doses are estimated to range from 8,500 r to 6,000 r in 7 to 9 days. Since 1934 external irradiation has rarely been used for the treatment of secondary nodes, and since 1936 block dissection of the neck has been practised for lesions of the anterior two-thirds of the tongue (groups (*a*) and (*b*)), even in the absence of palpable nodes.

The 5-year cure rates are: group (*a*); without palpable nodes 16% of 42 cases, with mobile nodes 15% of 40 cases; group (*b*), without nodes 31% of 336 cases, with mobile nodes 10% of 219 cases; group (*c*), without nodes 15% of 87 cases, with mobile nodes 11% of 136 cases. The 10-, 15-, and 20-year cure rates and incidences of late recurrences are also given. The best results (5-year cure rate, 25%) were obtained in a series of 362 cases treated by radium implantation with block dissection. The nodes were found to be invaded in 63% of these cases. Two cases of post-irradiation sarcoma of the tongue are recorded. *J. L. Dobbie*

2312 (*b*). **End Results of Treatment of Cancer of the Tongue**
E. BERVEN. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **63**, 712–715, May, 1950.

In analysing the results of treatment of cancer of the tongue at Radiumhemmet, Stockholm, between 1921 and 1942, the author divides the cases treated into two groups: (1) those treated in the period 1921-30 by surface and early implantation methods; and (2) those treated in the period 1931-42 by teleradium and electrocoagulation. For the latter method five 5-cm. fields are used covering the primary and the neck on the affected side. A tumour dose of 5,000 to 5,500 r is given in 15 to 20 days. In most cases a small remnant is apparent 2 or 3 months later and is treated by bipolar coagulation.

In the first series 136 patients were treated, with a relative cure rate of 20%. In the second, 267 patients were treated, with a relative cure rate of 28%. Survival rates for the second series up to and over 15 years are also given. In the second group of 267 patients treated, 103 had no clinical metastases on admission or later, 130 had metastases, and 34 developed metastases after admission. The 5-year cure rates were, respectively, 52%, 15%, and 6%. Only 24 block dissections were performed and the author suggests that more frequent surgery might possibly improve results. *J. L. Dobbie*

2312 (*c*). **Treatment of Cancer of the Tongue**
S. CADE. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **63**, 716–718, May, 1950.

This report is based on the study of 365 cases of cancer of the tongue treated over a period of 25 years at the Westminster Hospital, London. The treatment of choice is with radium, except in about 7% of cases.

Implant methods are used for the anterior part of the tongue, teleradium for the base and adjoining parts. Moulds are occasionally used. The implant dose has varied between 6,000 r and 9,000 r and the dose rate between 30 and 75 r per hour; a treatment period of 7 days is now used. The teleradium dose has been 5,000 to 6,000 r in 4 to 6 weeks. Secondary nodes have been treated by block dissection, or by irradiation methods in inoperable cases.

Four analytical tables of results are given. Over the whole group the 5-to-15-year survival rate is 27%, but in the period 1924–39, 220 cases were treated, with the following 5-year survival rates: early cases, 17 out of 30 (57%); without secondary nodes, 20 out of 60 (33%); with secondary nodes, 12 out of 130 (9%).

J. L. Dobbie

2312 (*d*). **End Results and Treatment of Cancer of the Tongue**

B. W. Windeyer. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **63**, 719–726, May, 1950.

The author gives five tables analysing the results of treatment in 243 cases of cancer of the tongue in the period 1931–42 at the Middlesex Hospital, London. For the whole group there was a 5-year cure rate of 21%. The best results were obtained in cases of cancer of the anterior two-thirds of the tongue without secondary nodes (31 survivors out of 70 cases (44%)). Cancer of the tongue makes up less than 2% of the total cancer cases registered at the Middlesex Hospital, and is decreasing in incidence. Treatment has been by radium implantation for tumours of the anterior two-thirds of the tongue, and by teleradium for those of the posterior third. A few cases of both types have been treated by *x*-ray therapy, and occasionally intraorally, but the results were found to be not so good as with teleradium.

Secondary nodes have been treated by block dissection, but only when palpable. Frequent follow-up examination is practised. In a considerable number of cases operable secondary nodes were treated by teleradium, but this policy has been abandoned in favour of block dissection for all operable nodes. Treatment by teleradium both for the posterior part of the tongue and for inoperable nodes is planned to deliver 6,000 to 7,000 r in 30 to 40 days. Radium implants are designed to deliver 6,000 to 9,000 r in 6 to 8 days.

An extensive summary of the Paterson–Parker dosage system is included, and great emphasis is placed on the radiographic measurement of implants, with the collaboration of the hospital physicist, in order to determine the dosage rate. *J. L. Dobbie*

2312 (*e*). **The Technique and Results of Treatment of Cancer of the Tongue with a 10 Gram Radium Beam Unit**

C. A. P. Wood. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **63**, 727–738, May, 1950. 17 figs., 5 refs.

The author gives a description of the 10-gramme radium beam unit designed and developed at the Medical Research Council's Radiotherapeutic Research Unit, Hammersmith Hospital, London, and of four accessories: a treatment caliper, a measuring caliper, a calculating table, and a dose contour finder. She then outlines the technique developed for the use of the unit in radiotherapy. A trial of selected fields is first applied to the patient by the therapist using the measuring caliper, and from the readings taken the resulting dose rate at the tumour and other points is calculated. The dose distribution is further investigated by means of the contour finder, and adjustments in planning are made in the light of this information. In these investigations the hospital physicist plays a large part. The intention is to deliver 6,000 r to the primary tumour and the regional lymph nodes in 42 days. Diagrams of 5-field, 4-field, and 3-field arrangements are given, showing also the resulting dose distribution.

A series of 182 unselected cases of carcinoma of the tongue in patients referred from other hospitals were treated. No patient was refused treatment. In most cases the disease was advanced and in more than half the patients the primary tumour was more than 4 cm. in diameter, while in only 8 cases was it less than 2 cm. The site of the primary was: anterior two-thirds 57%, posterior third 43%. Palpable lymph nodes, judged to be malignant, were present in 64% of cases. In no case was a neck dissection done. Recession of secondary masses was, as often as not, more rapid than that of the primary growth, and it is concluded that secondary nodes are not more resistant to radiation than primary growths. In a few cases a residual primary mass was treated also by radium implant or diathermy excision as soon as possible after the teleradium.

The results of treatment are given in detail in a table and a statistical diagram. For the 66 patients without secondary nodes the 5-year survival rate was 35%; for the 166 with secondaries it was 17%. *J. L. Dobbie*

2313. **Clinico-statistical Report on Oral and Pharyngeal Carcinoma Treated from 1928 to 1945. Part II. Results of Radiotherapy in Carcinoma of the Soft Palate.** (Rendiconto clinico-statistico dei carcinomi della bocca e del faringe trattati dal 1928 al 1945. II. Risultati della radioterapia nei carcinomi del palato molle (84 casi))

A. Perussia. *Radiologia Medica* [*Radiolog. med., Torino*] **36**, 378–412, May, 1950. 1 fig., 14 refs.

A series of 84 cases of carcinoma of the soft palate were treated in the University of Milan between 1928 and 1945. Cases are divided into two groups: (1) Carcinoma of soft palate in the strict sense. (2) Other tumours, including those of the anterior pillar of fauces and those arising from the retromalar space. The most satisfactory treatment was by radium implantation or *x*-irradiation by means of an intraoral tube combined with excision of lymph nodes involved. Clinical varieties of these groups of carcinoma are discussed with special reference to metastases and to the most important factors in prognosis. Treatment by surgery and radiation is outlined.

The author's main points are as follows. (1) In cases of limited primary tumour of the soft palate, he recommends radical excision by cautery followed by irradiation,

the dose of *x* rays being similar to that given in cases not operated upon. (2) In all other cases the only hope of cure lies in radiotherapy. (3) For therapy of a primary tumour, intraoral radium implantation gives the best uniformity of irradiation and is the treatment of choice. Direct transoral *x*-ray therapy is less certain. Employment of teleradium and long-distance *x*-ray therapy is not justified in these cases. (4) In advanced cases with extrinsic induration, uniform irradiation by intraoral radium implantation presents considerable difficulty. External irradiation is recommended here. (5) Treatment of lymph-node involvement is surgical. (6) In cases in which lymph-node involvement is not evident, careful and scrupulous follow-up is imperative. In dubious cases surgical treatment is indicated. (7) In the presence of suspected or evident lymph-node involvement, in which operation is for any reason impracticable, the author employs radiotherapy. (8) Post-operative irradiation of the neck after block dissection of lymph nodes has been abandoned by the author, because in his opinion this practice was ineffective. *L. G. Capra*

2314. **The Radiotherapy of Bone Metastases from Carcinoma of the Breast.** (Die Röntgentherapie der Knochenmetastasen nach Mammacarcinom)
C. FRIED. *Radiologia Clinica* [*Radiol. clin., Basel*] **19**, 129–158, May, 1950. 7 figs., 25 refs.

Hormonal therapy, including *x*-ray sterilization, has only an uncertain, partial, or temporary effect on bone metastases from breast cancer. Local deep *x*-ray therapy is regarded by the author as the treatment of choice, resulting in relief of pain, regeneration of bone, and prolongation of life; this last point has been insufficiently stressed in the literature. *X* rays (200 kV with a half-value layer of 2·1 mm. Cu) were used in a series of 37 cases, almost all with 3 to 6 metastases. The usual dose was 200 r daily (measured in air). Relief of pain may follow as little as 600 r, possibly owing to an effect on peripheral inflammation involving nerves; more advanced cases need 1,500 to 2,000 r for relief. These doses, however, are minimal and are liable to be followed by recurrence of pain in a few months; more radical dosage is therefore advisable to achieve a lasting effect on the tumour cells. For cervical vertebrae 3,000 r is recommended; for dorsal or lumbar vertebrae, pelvis, or hip, 5,000 r. For multiple lesions the total dosage is necessarily large—in one case, over 28,000 r. For vertebrae two angled converging fields are used; if there are other lesions also to be treated it may be necessary to give partial dosage and to complete the course later. If pain is not relieved the reason lies in radioresistance of the tumour. There were only 2 patients in the author's series in whom treatment with local deep *x* rays failed to relieve pain, and both died soon after; failure is therefore to be regarded as a bad prognostic sign. Illustrative cases are described and skiagrams are reproduced showing bony regeneration; healing begins to be visible in 6 to 8 weeks, but takes months to be complete.

The average length of survival among the 37 patients was 13·3 months, as compared with about 5 months for non-irradiated cases (from the literature); 15 patients survived more than one year, 8 of whom have since died, the remaining 7 patients having survived for an average period of 2 years 8 months after treatment. *J. Walter*

2315. **The Role of Connective Tissue in the Radiation Reaction of Tumours**
B. JOLLES and P. C. KOLLER. *British Journal of Cancer* [*Brit. J. Cancer*] **4**, 77–89, March, 1950. 12 figs., 36 refs.

The biological basis of radiation reactions in tumours is discussed and the need to study these effects in all components of the tumour and not in the cells alone is stressed. The radiation reaction was examined by histological and cytological techniques in 18 cases of accessible tumour treated by the "sieve" or "chessboard" method, in which the tumour is divided into a number of alternating exposed and protected areas 1 to 2 cm. in diameter. To give full treatment, two such sieves are used alternately, the second differing from the first in that the order of transparent and opaque areas is reversed, so that finally the whole area is equally exposed. By employing only one sieve, however, the effects of indirect irradiation on the protected areas may also be studied.

The effects of direct and indirect radiations are shown in tabular form and are well illustrated. In addition to the injuries induced in tumour cells by direct irradiation, fibrosis and a condition resembling inflammation are induced in the stroma. When the single sieve is used cell changes and stroma reactions are reduced in the exposed areas, but changes are induced in the stroma of the protected area, although no direct injuries are observed in the tumour cells. When the alternating-sieve technique is used the reaction of the tissues becomes uniform throughout the tumour, but it is claimed that specific alterations are induced in the irradiated areas which enhance tumour destruction. *M. C. Tod*

2316. **Roentgen Therapy in Neuroblastoma. A Review of Seventy-three Cases**
M. H. WITTENBORG. *Radiology* [*Radiology*] **54**, 679–688, May, 1950. 4 figs., 8 refs.

At the Children's Medical Centre, Boston, 143 neuroblastomata were recorded up to 1949. Many received a variety of therapeutic measures; the 73 cases analysed in this paper are those in which clinical and histological diagnoses are available and which were treated by *x*-irradiation. In general, localized tumours were treated by surgery whilst those unsuitable for surgery were treated by irradiation.

Of the tumours 80% occur within the first 5 years of life. The primary site was most frequently the upper abdomen, then the pelvis, whilst in 8% it remained unknown. In 60% metastases were present at the time of diagnosis, the skeleton being most commonly affected, although 8 patients had metastases limited to the liver, 4 to the mediastinum, 3 to liver and mediastinum, and 1 to liver and skin. Twenty patients with metastases all died within a year; one patient lived for 10 years after the diagnosis was established, and 2 are alive and well 12 and 16 years after operation. Out of 12 patients treated by operation alone, in 7 the tumour was confined

to the upper abdomen and 6 survived 3 or more years. Of 11 patients treated by operation and post-operative irradiation, 9 had localized tumours and 6 of these have survived 3 or more years, although 6 of them had incomplete excisions. Four of the latter have been followed up for 3 to 9 years. Probably for no other malignant tumour does post-operative irradiation offer so promising an outlook after incomplete excision. In 22 cases only biopsy and irradiation were used; 6 patients are alive and well after 2 to 12½ years; one died during therapy from uraemia and 15 died from metastases within 1 year.

Almost all the patients who survived received unusual tumour doses of 800 to 1,200 r in 10 to 14 days, usually followed by a second course in 3 months. Post-operative irradiation was begun within a day of operation; initial doses of the order of 200 r in air and total doses of 1,400 to 1,800 r in air delivered in 7 to 10 days did not affect wound healing. The limiting dosage factor in children is not the skin but the haematopoietic tissue.

I. G. Williams

2317. **"Azulol", a New Synthetic Preparation for Radiation Skin Reactions.** [Azulol, ein neues synthetisches Hautpflegemittel für strahlenbedingte Hautreaktionen)
W. ROECKERATH. *Strahlentherapie* [*Strahlentherapie*] **82**, 253–256, 1950. 6 refs.

The recently synthesized active principle of camomile, a member of the azulene group, was tested in a concentration of 10 mg. per 100 g. in a petrolatum–lanoline base; this is twenty times the concentration in camomile ointment. It had no abnormal effects on normal skin. When it was used as a local application to heavily irradiated skin undergoing moist desquamation and excoriation, the effects were striking. Burning and itching were relieved in ½ to 1 hour. Re-epithelization was complete in 3 to 5 days, including repair of mucocutaneous junctions (mouth, vulva, anus). Subsequent pigmentation was not different from that usually seen. A surprising finding was that if the ointment was applied to the skin from the start of the course of *x*-ray therapy the skin reaction appeared earlier than usual. The ointment is considered to be the best application available for radiodermatitis.

J. Walter

RADIODIAGNOSIS

2318. **The Radiological Assessment of the Normal Aqueduct and 4th Ventricle**
D. SUTTON. *British Journal of Radiology* [*Brit. J. Radiol.*] **23**, 208–218, April, 1950. 15 figs., 26 refs.

In 100 normal subjects the fourth ventricle was examined radiologically at the National Hospital for Nervous Diseases, London. The radiological techniques used were air encephalography, air ventriculography, and positive-contrast ventriculography, 1·0 to 1·5 ml. of "myodil" being employed for the latter. Two reference lines are described: (1) The Swedish line, (*Acta radiol., Stockh.*, Suppl. 24, 1935), running from the tip of the dorsum sellae through the lower part of the aqueduct to the skull vault. This is divided into thirds; the aqueduct lies at the junction of the proximal and middle thirds of this line. Significant backward displacement of the aqueduct, as in pontine lesions, can thus be detected. (2) Twining's line (*Brit. J. Radiol.*, 1939, **12**, 385) joining the tuberculum sellae and the internal occipital protuberance. This cuts through and passes just below the centre of the 4th ventricle at its mid-point.

The claims made by the originators of these two lines were confirmed completely. Absolute measurements were made as follows: (*a*) distance between the dorsum sellae and the aqueduct, 2·9 to 4·1 cm.; (*b*) distance from the dorsum sellae to the floor of the 4th ventricle, 3·1 to 4·1 cm.; (*c*) length of the aqueduct (this accorded well with the anatomical figure of 1·5 cm. in the few cases in which it could be measured); (*d*) width of the aqueduct (variable, but usually 0·2 cm. at 1·0 cm. below its upper end); (*e*) height of the 4th ventricle, 1·3 to 2·1 cm. (usually lessened in cases of pontine tumour); (*f*) distance from fastigium to mouth of the aqueduct (a wide range of measurement from 3·4 to 5·1 cm., but in cases of pontine tumour the measurement was well outside the maximum); (*g*) ventricular angle (obtained by synthesizing tracings from relevant films), being the angle between (1) a line joining the mid-point of the floor of the 4th ventricle to the mouth of the aqueduct, and (2) another line joining the lowest points of the floor of the 3rd ventricle; always between 85 and 95 degrees, and providing an index of the upward displacement of the back end of the 3rd ventricle. The author found that the relative measurements provided by Twining's line and the Swedish line were often of more value than the absolute measurements. He also elicited the fact that, even in the relatively small number of cases under review, the range of normal extended beyond the limits given by other investigators.

G. A. Stevenson

2319. **Simultaneous Occurrence of Pulmonary Tuberculosis and Pulmonary Carcinoma.** (Gleichzeitiges Vorkommen von Lungentuberkulose und Lungenkrebs)
E. MUNTEAN and R. AMON. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortsch. Röntgenst.*] **73**, 156–163, June, 1950. 9 figs., 30 refs.

Cases in which pulmonary tuberculosis and bronchial carcinoma occur simultaneously are reported to be on the increase. These cases present serious difficulties for the radiologist, because the pulmonary tuberculosis may completely mask the carcinomatous changes or a small carcinoma may cause extensive metastases masking the tuberculous lesion. The authors' observations from January, 1948, to May, 1949, include 86 cases of bronchial carcinoma; in 9 of these there was also active tuberculosis and in two inactive tuberculosis.

The authors divide their cases into three groups. The first group includes cases in which there is no evidence that one process causes or influences the other one. Some authors consider association of these two processes to be accidental, and believe that tuberculosis is not a pre-cancerous disease. The tuberculosis is usually inactive in these cases. The low incidence of the

combination is probably due to the short life of tuberculous patients. Tuberculosis is associated with carcinoma in 12 to 20% of all cases. The second group comprises cases in which anatomical and histological examination shows that carcinoma originated in the old infiltrating tuberculous scar or in the wall of a cavity. The carcinoma is usually small and peripheral. A fibrous scar can be followed up to the pleura, which is free from tumour. In the neighbourhood of the centre, carcinoma nests and necrotic zones are often present and so are tuberculous granulations. This shows that the tuberculous scar was the primary condition on which carcinoma supervened. The third group is that in which inanition due to carcinoma has activated old tuberculous foci. *W. J. Czyzewski*

2320. **The Radiological Appearances of Bronchial Dilatation in the Adult as Seen on the Plain Film.** (Les aspects radiologiques prébronchographiques des dilatations des bronches de l'adulte)
H. Brocard, R. Pichard, and H. J. Bernard. *Presse Médicale* [*Pr. méd.*] **58**, 469–471, April 26, 1950. 15 figs.

In contrast to the previously generally accepted belief that the radiographic signs in bronchiectasis are scanty while the clinical picture may be very suggestive, the authors advance the view that the signs in routine straight radiographs are often more definite than the clinical manifestations. The most characteristic changes are vesicular and spotty shadows. Reticular shadows are less typical, while cavitary shadows and shrinking pulmonary fibrosis are less frequently seen. Great care is necessary in the interpretation of an accentuated broncho-vascular design. *A. Orley*

2321. **The Radiological Demonstration of Apical Lung Lesions.** [In English]
E. G. Hoffstaedt. *Radiologia Clinica* [*Radiol. clin., Basel*] **19**, 164–169, May, 1950. 6 figs., 5 refs.

2322. **Retrograde Arteriography in the Diagnosis of Cardiovascular Lesions. II. Coarctation of the Aorta**
N. E. Freeman, E. R. Miller, H. B. Stephens, and M. B. Olney. *Annals of Internal Medicine* [*Ann. intern. Med.*] **32**, 827–841, May, 1950. 6 figs., 8 refs.

Angiocardiography by the ordinary intravenous route is often unsatisfactory for the precise demonstration of narrowing of the aorta. Because of the desirability of obtaining better pictures before operation, the authors resorted to the injection of " diodrast " into the common carotid artery exposed just above the inner end of the clavicle. The artery is held in a segment of rubber tubing which prevents an upward flow of the contrast medium into the brain. A dose of approximately 1 ml. 70% diodone per kg. body weight is used, up to a maximum of 50 ml. A 16-gauge or 18-gauge needle is inserted into the artery in a proximal direction, and after injection of the contrast medium exposures are made. The first film is taken immediately upon completion of the injection and two or three further films are rapidly exposed at intervals of 2 seconds. As would be expected, reasonably satisfactory pictures are obtained by this technique, and by accurate visualization of the thoracic aorta it is estimated that 4 out of 16 patients studied were saved unnecessary exploratory thoracic operation. The degree of stenosis can be more accurately estimated, and examples are given of unusual position and exceptional length of the narrowed area. [This procedure involves major surgery, which may possibly be avoidable by other techniques such as passage of a catheter into the aorta via the arm arteries, or the injection of a dye into the pulmonary artery during cardiac catheterization.]
J. McMichael

2323. **A Comparison of Electrokymography and Roentgenkymography in the Study of Myocardial Infarction**
S. Dack, D. H. Paley, and M. L. Sussman. *Circulation* [*Circulation*] **1**, Part I, 551–563, April, 1950. 7 figs., 19 refs.

The clinical usefulness of electrokymography in diagnosis of myocardial infarction is said to be demonstrated by the presentation of records obtained in 2 cases. In the first, the classical symptoms and clinical features of cardiac infarction were present; the diagnosis was supported by typical electrocardiographic findings and by clinical evidence of cardiac aneurysm; the electrokymogram showed paradoxical pulsation of the lower left ventricular border. In the second, the clinical features were those of congestive failure of unknown aetiology; the electrocardiogram showed no evidence of cardiac infarction or ischaemic heart disease, and there was no necropsy. The electrokymogram is said to show the infarct [but no proof of its existence is given.]
Paul Wood

2324. **Death following Angiocardiography**
C. T. Dotter and F. S. Jackson. *Radiology* [*Radiology*] **54**, 527–533, April, 1950. 6 refs.

This survey is based on statistics obtained from various centres in the United States, Canada, Great Britain, and Sweden. Out of a total of 6,824 angiocardiographies 26 patients died after the procedure.

The number of angiocardiographies carried out in the United States was 5,961; in these 18 patients died. The corresponding number for Great Britain was 413; in these 7 patients died. In Sweden only one patient died out of a total of 450 angiocardiographies.

No deaths were recorded among patients with a healthy heart, except in one case of arterial renal disease. Three deaths occurred in mongols. The commonest form of death was sudden respiratory arrest immediately or shortly after the injection of the contrast medium. The cause of death was rarely found at necropsy. In several cases there was evidence of pulmonary oedema. Subdural haemorrhage was present twice.

The available data do not indicate that the nature of the contrast medium, the number of injections, the premedication, or use of general anaesthesia influenced the mortality from the procedure. The incidence of death was higher in children, in patients with congenital heart disease, in patients receiving larger doses of the contrast medium, and in patients examined in the horizontal position. *A. Orley*

2325. **The Importance of Renal Function Tests before and after Angiocardiography.** (Importance du bilan rénal avant et après l'angiocardiographie)
E. Donzelot, R. Heim de Balsac, M. Durand, J. E. Escalle, C. Metianu, and L. Préaux. *Archives des Maladies du Cœur et des Vaisseaux* [*Arch. Mal. Cœur*] **43**, 410–414, May, 1950. 3 refs.

Injection of a radio-opaque iodine salt for angiocardiography into 106 children with congenital heart disease caused a transitory impairment of renal function in 40% of cases as judged by changes in blood urea level and phenolphthalein excretion and by the presence of blood and casts in the urine. The authors advise using the least amount of iodine salt possible; the subject should rest for at least a week afterwards. They stress the value of oxygen for cyanosed patients after angiocardiography. *D. Verel*

2326. **Chordomas: a Roentgenologic Study of Sixteen Cases previously Unreported**
E. H. Wood and G. M. Himadi. *Radiology* [*Radiology*] **54**, 706–716, May, 1950. 8 figs., 19 refs.

Chordomata are neoplasms of relatively low malignancy which arise from remnants of the notochord. They are rare tumours and may occur at any point in the axial skeleton from within the skull to the coccyx. They are twice as common in men as in women. The cranial chordomata appear most frequently during the third and fourth decades of life, whereas the sacral tumours are seen more commonly during the fifth and sixth decades. Metastases have been reported only from tumours arising in the sacro-coccygeal area. The present report is based on the findings in 16 patients seen over the last 20 years at the Columbia–Presbyterian Medical Centre, New York. The tumours appeared or occurred in the clivus in 7 patients, in the nasopharynx in one, in the vertebrae in 5, and in the sacro-coccygeal region in 3.

Chordomata of the clivus cause osteolysis of the sphenoid bone in the great majority of cases. The tumour commonly extends into the sphenoidal sinuses, often into the nasopharynx, and occasionally into the ethmoid region. Pneumoencephalography and ventriculography are helpful in demonstrating the retrosellar position of the tumour. In addition, the third ventricle is usually displaced upward, while the aqueduct of Sylvius and the fourth ventricle are displaced backward. The tumour is outlined by gas in the subarachnoid cisterns. In contradistinction to the findings of other authors, calcified particles were demonstrated in 6 out of 7 cases of clivus tumour. Vertebral chordomata produce bone destruction in two or more vertebrae, the destructive process being most obvious in the bodies, although the neural arches may also be involved. As the tumour extends from one vertebra to another there is loss of joint space. In addition the tumour masses may extend into the soft tissues at either side of the vertebral column, giving rise to an opacity. It is thus necessary to exclude tuberculosis or pyogenic osteomyelitis. Collapse of the vertebral body is a common feature. In 2 of the 5 cases reported an osteoblastic reaction was present in addition to the osteolysis. In the 3 cases of sacral tumour reported osteolysis was present in one or more segments of the sacrum and coccyx. A soft-tissue mass was demonstrated radiologically in 2 of the 3 cases, and in all cases calcification or fragmented bone was visible.

Conservative surgical excision and external irradiation are the procedures usually employed in treatment. A favourable response to *x*-ray therapy may be expected in a small percentage of cases, with gratifying palliative results. *L. G. Blair*

2327. **Diastematomyelia. Transfixation of the Cord or Cauda Equina with Congenital Anomalies of the Spine**
E. B. D. Neuhauser, M. H. Wittenborg, and K. Dehlinger. *Radiology* [*Radiology*] **54**, 659–664, May, 1950. 8 figs., 10 refs.

Diastematomyelia is a developmental defect of the neural axis and spinal column with sagittal division of segments of the cord, the cord or cauda being transfixed by an osseous or fibro-cartilaginous septum. Some 51 cases have previously been described in the literature, in none of which the diagnosis was made pre-operatively. The authors report 12 cases proved by operation at the Children's Hospital of Boston, Massachusetts, in 10 of which the diagnosis was made pre-operatively. Six other patients suspected, on the basis of the *x*-ray findings, of having diastematomyelia are awaiting operation. Nine of the proved lesions occurred in the cord and 3 in the cauda equina.

The transfixation fixes the cord in a low anatomical position and the resultant traction produces neurological disturbances. There may be evidence of impaired innervation to the lower extremities or disturbance of sphincter control. Usually no abnormality is obvious at birth, but with increasing age the child develops a limp, and atrophy of one or both legs, with associated bone changes, may be noted. *X*-ray examination shows a widening of the neural canal and the interpedicular spaces which may extend over 3 to 6 adjacent spinal segments. The involved pedicles are not narrowed, and hence the appearances suggest congenital widening of the spinal canal rather than recent pressure erosion. When the septum which divides the cord is osseous it is best seen in a film made in the antero-posterior projection, and may be recognized as a small, linear or irregular fragment of bone, lying in the midline of the neural canal. Various other anomalies of the vertebral bodies and arches usually exist, especially at or near the area of diastematomyelia. If the septum is fibro-cartilaginous it will be necessary to carry out myelography to clinch the diagnosis. In these cases a linear filling defect will be seen in the centre of the column of opaque medium. *L. G. Blair*

2328. **The Diagnosis of Hydrops Foetalis**
J. L. Boldero and F. H. Kemp. *British Journal of Radiology* [*Brit. J. Radiol.*] **23**, 219–224, April, 1950. 10 figs., 2 refs.

The authors accept the "Buddha" position of the foetus as evidence of an advanced degree of hydrops foetalis, but they feel that diagnosis of hydrops may confidently be made at a much earlier stage in the

presence of the following: (1) Straightening of the normal kyphosis of the foetal spine with extension of the neck. (2) Radiographic evidence of hydramnios. (3) Evidence of iso-immunization of the mother. They are satisfied that hydramnios alone does not cause the foetus to assume this straight position and that it is purely the mechanical result of the distension of the foetal abdomen by ascites and of the oedema of the soft tissues of the neck, both of which may occur relatively early in the development of the hydropic state. Straightness of the foetal spine and even extension of the neck may, however, be due to other causes: (1) Adaptation to the presence of a second foetus or other intrauterine structure such as an abnormally large placenta. (2) An intra-abdominal foetal tumour of renal or hepatic origin may straighten the foetal spine, or a thyroid tumour may extend the neck.

During a period of one year, the authors radiographed all Rh-negative mothers attending the Radcliffe Infirmary, Oxford, in the later weeks of pregnancy, with evidence of iso-immunization. Changes indicative of hydrops were found in 3 out of 18 such cases, the 15 other patients appearing normal radiographically. All but one of these 15 patients gave birth to live babies who survived with or without replacement transfusion. The authors stress that the degree of curvature of the foetal spine and extension of the neck can be assessed only after a lateral view of the foetus has been obtained.

J. Rabinowitch

2329. **The Prenatal Radiological Diagnosis of Hydrops Foetalis**

E. Samuel and J. Cohen. *British Journal of Radiology* [*Brit. J. Radiol.*] **23**, 225–230, April, 1950. 7 figs., 9 refs.

Hydrops foetalis is characterized by marked generalized oedema and anaemia associated with accumulation of fluid in the pleural and peritoneal cavities. In addition, partly as the result of extramedullary erythropoiesis and partly because of oedema, there is an enlargement of the liver and spleen. Examination of the blood shows immature erythrocytes. There is an enlarged and oedematous placenta.

The radiological signs of hydrops foetalis can be subdivided into two groups: (*a*) those characteristic of hydrops foetalis, that is, due to anasarca and the exudate into the body cavities; (*b*) those changes common to all types of erythroblastosis foetalis.

Javert in 1942 drew attention to a sign noted before—the formation of a double shadow round the bones of the cranial vault. He named this sign the "halo sign", but radiologists, who see many cases, are inclined to disregard the value of this sign, as it is met with in the case of many normal, well developed foetuses.

Alteration in the spinal curvature is present because of general ascites and enlargement of liver and spleen. This causes straightening of the normal curvature of the spine, and the straightening of the spine in part contributes to the Buddha-like appearance of the foetus, the legs being flexed at the knees and partly extended at the hip-joints. Hartley has doubted the significance of this sign, and has shown cases where such a position may be adopted by a normal foetus.

Osteopetrosis in the long bones has been described in this condition. The authors conducted experiments in order to demonstrate whether the osteopetrosis noted was real or apparent. The latter might be produced by oedema of the tissue as opposed to true increase in the density of the bones. They deduced that the fluid increase in the soft tissues contributed in part to the increased density of the skeleton. There was no increase in the amount of calcification or density of the bone. The bone marrow was hyperplastic and showed marked erythropoiesis. A case described showed all these radiological signs, except the halo sign. They were not able to demonstrate an enlarged and swollen placenta radiologically. An interesting finding in their case was the very low anti-Rh antibody titre, which remained consistently below 1 in 32, in spite of the very pronounced radiological findings.

J. Rabinowitch

2330. **The Value of Tannic Acid Enema and Post-evacuation Roentgenograms in Examination of the Colon**

A. C. Christie, F. O. Coe, A. O. Hampton, and G. M. Wyatt. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **63**, 657–664, May, 1950. 5 figs., 8 refs.

The authors discuss the difficulties of demonstrating polyps and small malignant lesions of the colon by means of the barium-enema *x*-ray examination and advocate the addition of tannic acid to the contrast medium as a means of obtaining a better post-evacuation mucosal pattern. They claim that this results in a complete mucosal picture of the whole colon, instead of the partial one commonly met with in post-evacuation films obtained in the normal manner. Their technique is as follows: 16 hours before examination 1 to 2 oz. (30 to 60 ml.) of castor oil is administered, followed 3 hours before the examination by a cleansing enema. Then, if the bowel is thoroughly clean, the barium-enema examination is carried out in the customary manner, except that 1 g. of tannic acid powder is added to every 100 ml. of the barium mixture. Stress is laid on the importance of carrying out the examination thoroughly, especially in all cases of rectal bleeding, manipulation, palpation, and spot films being used to the full. Post-evacuation films are taken, and patience must be exercised in waiting until evacuation is complete and the mucosal pattern of the whole bowel displayed. The authors claim that the tannic acid produces greater contraction of the colon and leaves a better coating of barium on the wall. This procedure is followed by air insufflation when necessary, and the whole examination is repeated if any suspicious area is seen on the films which was not noted on screening. The authors have made 4,225 examinations with this technique, resulting in the diagnosis of 40 polyps (10 of which were found to be malignant) and 38 carcinomata of the colon [total number of patients not stated]. In only 2 of the 40 cases was the polyp demonstrable by proctoscopy and 6 patients were not subjected to operation. Of the remainder, the polyp was found at operation in all but one case, in which, however, it was subsequently found in the stools, having been detached from its pedicle by too vigorous manipulation.

G. A. Stevenson

Pathology

EXPERIMENTAL

2331. **A Study of the Changes in the Brain in Experimental Internal Hydrocephalus**
S. N. De. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 197–208, April, 1950. 16 figs., 40 refs.

The author produced hydrocephalus in adult Wistar rats by the intracisternal injection of 0·2 ml. of a 20% aqueous suspension of indian ink. The animals were killed after 4, 6, 8, or 12 weeks and hydrocephalus was found to be present in 31 out of 59. Other methods of producing hydrocephalus, by the injection of fibrin, transplantable tumour, or *Mycobacterium tuberculosis*, were less successful and were abandoned. Injections of Prussian blue showed that the hydrocephalus was of the external and communicating type, and was caused by the adhesion of the pia and arachnoid over the basal cisterns. The enlargement involved first, and was always maximal in, the anterior horns of the lateral ventricles. This enlargement was compensated for by atrophy of the septum pellucidum, corpus striatum, and corpus callosum. In these sites Pickworth staining showed ischaemia due to a loss of capillaries and precapillaries. There were also interstitial oedema, chromatolysis, and nuclear displacement at these sites. Astrocytes were atrophic near the ventricles and hypertrophied farther away. Nerve fibres showed axon irregularities and demyelinization. All these changes are attributed to ischaemia caused by a rise in cerebrospinal-fluid pressure above the level of the capillary blood pressure. Fatty change and microglial reaction were not observed, and their occurrence in human infantile cases is correlated with cerebral expansion and possible tearing of fibres. The choroid plexus remained unchanged, and this is regarded as a result of its higher capillary pressure. It showed no mitochondrial change, which the author takes as evidence against the theory of secretion.

C. V. Harrison

2332. **Allergic Encephalitis and its Possible Relationship to Human Disease**
J. H. Peers. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 503–514, June, 1950. 7 figs., 22 refs.

A detailed historical survey is given of the attempts which have been made to produce allergic encephalitis and the method by which the technique was evolved. There is also a well-illustrated description of the histological picture of the disease. A comparison is drawn between the lesions in experimental disease and the lesions of acute disseminated encephalomyelitis in man. Points of similarity include the location of lesions around small veins, the presence of perivascular round-cell infiltration, the predilection in most cases for the white matter, and the presence of partial demyelination, usually perivascular, which is accompanied by perivascular proliferation of the microglia. In the experimental disease the mortality is much higher than in acute encephalomyelitis in man, being over 90% in monkeys as opposed to between 10 and 30% in human post-vaccinal encephalitis. No lesions resembling those of human disseminated sclerosis have as yet been detected in animals surviving the acute stage of the experimental disease.

The nature of the encephalitis-producing agent is discussed, and the results of attempts to remove this factor from rabies vaccine made from rabbit-brain emulsion are given. The addition of a small quantity of calcium acetate to a watery suspension of benzene–ether extracted brain tissue removed the encephalogenic factor. Other experiments, which are being continued and extended, have shown that this factor is water-soluble and capable of dialysis through a "cellophane" membrane.

Ruby O. Stern

2333. **Mechanisms of Edema Formation in Chronic Experimental Pericarditis with Effusion**
A. P. Fishman, J. Stamler, L. N. Katz, A. J. Miller, E. N. Silber, and L. Rubenstein. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 521–533, May, 1950. 1 fig., bibliography.

Chronic pericarditis with effusion was produced in 15 dogs by the introduction of irritative "cellophane" into the pericardial sac. Death from congestive circulatory failure occurred in 6 to 44 days, post-mortem examination showing a massive sero-sanguineous pericardial effusion and a thick, rigid pericardium. Ascites, hydrothorax, pulmonary congestion and oedema, nutmeg liver, and peripheral pitting oedema were present in most animals.

The post-operative course fell into three phases. In the first there was a progressive rise in peripheral, central, and renal venous pressures. Renal plasma flow and glomerular filtration rate were normal, and plasma volume and thiocyanate space were unaltered. The sodium clearance test showed a significant decrease, indicating increased tubular reabsorption of sodium and water. The resting cardiac output was maintained at normal levels. A persistent tachycardia developed after 24 to 48 hours. In the second phase the effusion had greatly increased and there was gross anasarca. As the effusion progressed to tamponade there was a steady rise in the peripheral venous pressure and an equivalent rise in central and renal venous pressures. Plasma volume and thiocyanate space were significantly increased. The resting cardiac output was still normal, but there was an increased difference between arterial and venous oxygen concentrations. Renal plasma flow and glomerular filtration rate were normal, but the sodium clearance was more impaired. There was a moderate fall in arterial blood pressure. In the third stage, which

preceded death by 24 hours, there was moderate to severe circulatory collapse, marked by prostration, weak pulse, fall in arterial pressure, and hyperpnoea. The peripheral venous pressure was greatly increased and the resting cardiac output considerably diminished. The arterio-venous oxygen difference increased, renal plasma flow and glomerular filtration rates fell, and the filtration fraction rose. The impairment in sodium clearance was marked, with considerable retention of administered saline. Plasma volume and thiocyanate space were increased and extreme anasarca was present.

The authors' interpretation of these observations is that the first response to increasing pericardial pressure is a rise in venous pressure before there are any changes in the volumes of intra- and extra-vascular fluids. With the increased heart rate the resting minute volume is maintained. When the intrapericardial pressure exceeds 10 to 15 cm. water the effective filling pressure of the right auricle is reduced and the resting cardiac output falls, eventually causing circulatory collapse. The increased hydrostatic pressure results in an extravasation of oedema fluid from the vascular tree but, because of the increased renal reabsorption of salt and water, the circulating plasma volume is maintained, there being a net increase in the salt and water content of the body. Preterminally the greatly increased venous pressure results in a failure to maintain the resting cardiac output, blood pressure and renal plasma flow fall, and sodium clearance is further impaired. Fluid retention is increased and circulatory embarrassment further aggravated. *M. Lubran*

2334. **The Induction of Rheumatic-like Lesions in Rabbits by Repeated Focal Infections with Group A Streptococci. Comparison with the Cardiac Lesions of Serum Disease**
G. E. MURPHY and H. F. SWIFT. *Journal of Experimental Medicine* [*J. exp. Med.*] **91**, 485–98, May, 1950. 37 figs., 39 refs.

This paper is supplementary to a previous paper by these authors (*J. exp. Med.*, 1949, **89**, 687), which described the production in rabbits of a state similar to that of rheumatic fever in man by a series of multiple successive skin infections with group A streptococci of several serological types. It consists of a generously and well illustrated comparison of material from the hearts of 7 such rabbits who died or were killed within a period of 8 to 15 days after the last injection, and from the hearts in 12 human cases of rheumatic fever. No bacteria were cultured from the sections nor were any streptococci seen. No comparable lesions were found in normal control rabbits or in those dying or killed after one intracutaneous or intravenous inoculation of living or dead streptococci. Twenty photomicrographs illustrate the lesions in rabbits and are compared with those of 19 carefully picked human lesions. The endocardial lesions are similar to the early palisading valvulitis in man, but the verrucae found in the human disease at a later stage are not seen.

The myocardial lesion " approximates almost, if not absolutely, that of rheumatic fever in man ", and so do the changes in the vessels. No periarteritis-like lesions are seen. After a review of published work on serum carditis with its accompanying periarteritis-like lesions, the authors conclude that the rabbit streptococcal lesions and those of rheumatic fever in man resemble each other closely, but are different in several respects from those of serum carditis in man and in animals.

[For the first time, something approaching rheumatic fever clinically and histologically has been produced in animals; that it should have been produced by this method is very strong evidence for Swift's hypothesis of the nature of rheumatic fever.] *E. G. L. Bywaters*

2335. **Quantitative Studies in Experimental Cardiac Hypertrophy.** (Quantitative Untersuchungen bei experimenteller Herzhypertrophie)
A. FRANK and E. A. SCHOTTE. *Zeitschrift für die Gesamte Experimentelle Medizin* [*Z. ges. exp. Med.*] **115**, 677–687, 1950. 7 figs., 4 refs.

A histological study was made of the hearts of 18 adult male guinea-pigs in which cardiac hypertrophy had been induced by 4 months' daily exercise [swimming—details not given]. After the intracardiac administration of histamine to ensure patency of all capillaries, indian ink was injected into the left ventricle. The capillaries and muscle fibres were then examined in sections of papillary muscle. No evidence was found of an increase in capillaries per unit area—in fact, the number of capillaries and of muscle fibres per unit area were less than in the hearts of control animals—but the cross-sectional area of the individual muscle fibres was increased. The finding that the fibres increase in size without a proportionate increase in capillaries was considered to indicate that the hypertrophied heart is likely to suffer from relative ischaemia during increased load.

R. A. Gregory

2336. **Mechanism of Ventricular Fibrillation.** [In English]
D. SCHERF, L. J. MORGENBESSER, E. J. NIGHTINGALE, and K. T. SCHAEFFELER. *Cardiologia* [*Cardiologia, Basel*] **16**, 232–242, 1950. 5 figs., 21 refs.

In experiments on dogs, topical application of aconite crystals to the surface of the ventricle led to the appearance of a ventricular tachycardia with a slowly increasing rate (ventricular flutter). The rate could immediately be restored to normal by cooling the area to which the aconite was applied. Withdrawal of the cooling thermode restored the tachycardia at once. Further stimulation by aconite until rates of over 332 were reached produced ventricular fibrillation, which was found to be totally unaffected by cooling. Experimental evidence was obtained that rapid electrical stimulation of one ventricle may lead to occurrence of repetitive extrasystoles in the contralateral ventricle; this is facilitated by cooling the remote centre. Arguments are given in support of the view that the cause of ventricular fibrillation lies in multifocal stimulus formation rather than in a circus movement. It is thought that with rapid stimulus formation at the centre activated by the application of aconite, the activity of one or more remote centres is aroused as soon as a critical rate is reached; ventricular fibrillation then results.

J. L. Lovibond

2337. **Transmural Migration of Intestinal Bacteria. A Study based on the Use of Radioactive *Escherichia coli***
F. B. SCHWEINBURG, A. M. SELIGMAN, and J. FINE. *New England Journal of Medicine* [*New Engl. J. Med.*] **242**, 747–751, May 11, 1950. 6 refs.

The authors had previously found that the treatment of uraemia by peritoneal irrigation with slightly hypertonic fluid sometimes, despite all precautions, resulted in a peritonitis due to *Bacterium coli*. Evidence suggested that the bacteria gained entrance to the peritoneal cavity by direct migration through the wall of the gut. Experimentally it was shown that intraperitoneal injections into dogs of a sterile irritating substance such as monoethanolamine oleate produced a coliform peritonitis. In uraemic dogs, long-continued irrigation of the peritoneum with hypertonic fluids resulted in peritoneal lesions from which *Bact. coli* and some allied organisms could be recovered. At the same time blood cultures were found to be sterile. Bacteria made radioactive by treatment with a solution of radioactive iodine (I^{131}) were then introduced into the gastro-intestinal canal to test further the hypothesis of transmural migration. Both living and dead washed radioactive *Bact. coli*, standardized for radioactivity, were used.

When such labelled bacteria were introduced by stomach tube before coliform bacteria had appeared in the peritoneal exudate the amount of radioactivity subsequently found in the exudate was small, but if organisms were already present in the exudate then the amount of radioactive substance subsequently recovered from the exudate was very considerable. The intravenous injection of radioactive bacteria after the exudate had become contaminated with coliform organisms resulted in a low degree of radioactivity in the exudate, indicating that organisms were not passing into the peritoneal cavity in any numbers from the blood stream. There was definite evidence of migration of both living and dead bacteria through the gut wall under the conditions of the experiment.

The results of this investigation indicate that therapeutic irrigation of the peritoneum in uraemic patients should be accompanied by the oral administration of a suitable antibiotic. *H. J. Bensted*

2338. **Confirmation of Presence of a Gastric Secretory Depressant in Gastric Juice of Humans**
C. M. BLACKBURN, C. F. CODE, D. P. CHANCE, and E. E. GAMBILL. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 233–236, May, 1950. 8 refs.

In 1939 Brunschwig reported that an alcoholic precipitate of human achlorhydric gastric juice would depress gastric secretion when injected intravenously into dogs (Brunschwig *et al.*, *J. clin. Invest.*, 1939, **18**, 415). This finding has been confirmed at the Mayo Clinic with alcoholic precipitates, prepared according to Brunschwig's technique, of the gastric juice of patients with pernicious anaemia and simple achlorhydria, and of normal subjects. Eighteen assays were made after intravenous injection into dogs with Heidenhain pouches, the response to repeated injection of histamine over a control period of 2 hours being compared with that obtained over a 3-hour period after injection of the precipitate.

The precipitate from cases of pernicious anaemia in a dose of 10 mg. produced a 60 to 80% fall in 4 cases, and that from cases of simple achlorhydria in a dose of 25 mg. gave a 55 to 75% depression in 6 cases, while a dose of 200 mg. of the latter resulted in complete achlorhydria on the one occasion on which it was given. Precipitates from normal gastric juice produced no significant depression on five occasions, and a fall of 41% and 43% twice. Untoward reactions included transient weakness, tachycardia, and vomiting with the 200-mg. dose, and with all doses a slight rise in rectal temperature not related to the degree of gastric depression. *K. Gurling*

2339. **A Lipase Reaction in Phagocytes from the Peritoneum of Rats toward Previously Stained Fat**
R. M. WOTTON, T. U. H. ELLINGER, and J. C. BARTONE. *Anatomical Record* [*Anat. Rec.*] **107**, 73–79, May, 1950. 19 refs.

A dose of 0·5 to 1·0 ml. of cod-liver oil saturated with Sudan IV was injected intraperitoneally into each of 26 white rats. The animals were killed traumatically at times varying from 1 to 6 hours after the injection. The abdomen was opened and smears were made by passing slides over the visceral and abdominal peritoneum. The slides were fixed in formalin and then treated in one of the following ways: (*a*) stained with Sudan IV and then processed by the Gömöri method for lipase identification; (*b*) processed by the same method without previous staining; or (*c*) stained without processing.

Phagocytes accumulated closely around the droplets of injected fat. The surface associations appeared to be a preliminary step towards fat absorption. At certain very small but clearly defined points on these cells fine streams of fat were seen entering the cytoplasm, being either single or multiple for any given cell. The slides processed for lipase identification showed a brown area where the cell touched the fat globule. This is taken as evidence that a lipase reaction may occur at the cell–fat interface, with the possibility of extracellular digestion of fat as part of the absorption process. Neither the age of the rat nor the length of time from the fat injection materially altered the picture. Smears made from control rats did not show this phenomenon.

Two types of cell participated in this reaction; the histiocyte and, more rarely seen, a cell resembling a fibrocyte with filose pseudopodia. The latter type of cell appeared less active in fat absorption, the fat being present in small droplets, whereas considerable quantities were seen in the histiocytes. *W. H. Horner Andrews*

2340. **The Effect of Restriction of Fluid Intake on the Production of Nephrosis in Rabbits**
W. B. WARTMAN, J. M. TUCKER, and R. B. JENNINGS. *American Journal of Pathology* [*Amer. J. Path.*] **26**, 389–395, May, 1950. 4 refs.

In a previous paper from this department (Northwestern University Medical School) it was shown that in

rabbits in which obstructive jaundice was caused, transient ischaemia of one kidney produced a bilateral nephrosis with dilatation of tubules, degeneration of epithelium, and pigment casts. Deprivation of water has now been shown to have no influence on this phenomenon. *D. M. Pryce*

2341. **Intravital Staining of Damaged Liver Cells. II. The Use of Dyes in the Study of Necrosis and Repair following Acute Chemical Injury**
W. L. Williams. *Anatomical Record* [*Anat. Rec.*] **107**, 1–11, May, 1950. 28 refs.

In mice the centrilobular hepatic cells injured by carbon tetrachloride were stained intravitally by two acid diazo dyes and by the sulphonated triphenylmethane dye, isamine blue. The staining of these cells was of cytoplasmic suffusion type, not granular deposition. These central cells were also very hypobasophilic (nuclei and cytoplasm). Many cells of the middle zones also showed loss of cytoplasmic basophilia but were not vitally stained.

Subsequent necrosis was limited to vitally stained cells of the central zones. Cytolysis occurred within 2 to 3 days after termination of treatment with carbon tetrachloride, at which time the cytoplasmic vital stain was aggregated into large particles or granules. These accumulations of dye remained attached to cytoplasmic remnants for as long as such were identifiable. The cytoplasmic remnants and the adhering dye became parts of fusion-type giant cells and were eventually phagocytosed by macrophages.

Mitoses of midzonal cells occurred as early as 48 hours after injection of carbon tetrachloride. These new cells replaced the necrotic central zones, and repair without fibrosis was essentially complete within 21 to 30 days.

The damaged central cells reacted in the same fashion to each of the three dyes. These dyes did not stain the cytoplasm or nuclei of parenchymal cells of normal livers although they were abundantly deposited as segregated granules in adjacent sinusoidal macrophages. The dyes served as adequate labels for hepatic cells irreversibly injured by carbon tetrachloride.—[Author's summary.]

2342. **Experimental Total Midzonal Hepatic Necrosis**
B. Black-Schaffer, D. S. Johnson, and W. G. Gobbel. *American Journal of Pathology* [*Amer. J. Path.*] **26**, 397–409, May, 1950. 7 figs., 11 refs.

The authors obtained an important experimental result which was completely unexpected. Rabbits made to lose about a quarter of their weight by administration of thyroid become, of course, more susceptible to the toxic action of chloroform. A wide band of central hepatic necrosis might be expected to develop when chloroform is injected subcutaneously into such animals in a dose of 0·1 ml. per kg., but this did not occur in the authors' experiments. Instead, the central cells were spared and the necrosis affected only the midzone. This result is inexplicable on a mechanical basis and suggests that zonal differences in function exist. *D. M. Pryce*

2343. **Bronchial Changes in Experimentally Induced Cystic Degeneration of the Pancreas**
P. V. Véghelyi, T. T. Kemény, and J. Sós. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **79**, 846–854, May, 1950. 8 figs., 2 refs.

Extensive bronchiectasis, consequent on chronic peribronchitis and destruction of elastic tissue, was found to occur in rats subjected to carbon tetrachloride poisoning; similar but less severe changes were observed also in several animals fed on deficient diets. In the pancreas in both groups dilatation of acini leading to cyst formation with fibrosis was prominent. The authors regard this as an inadequate basis for deductions concerning the pathogenesis of fibrocystic disease of the pancreas, but reject the idea of a purely irritative process. *M. Baber*

2344. **Factors affecting the Number of Tumor Metastases. Experiments with a Transplantable Mouse Tumor**
I. Zeidman, M. McCutcheon, and D. R. Coman. *Cancer Research* [*Cancer Res.*] **10**, 357–359, June, 1950. 6 refs.

A preliminary determination was made of the relation between the number of viable tumour cells injected intravenously into mice and the number of resultant tumours in the lungs. A 100% transplantable sarcoma in C57 [black?] mice was used. Tumour tissue was forced through a wire-mesh screen, suspended in a mixture of equal parts of serum and saline, and allowed to sediment for 10 minutes. Viable cells in the supernatant were counted in a dilute solution of trypan blue. About 6% of the suspended cells were considered to be viable. Serial dilutions of the suspension were then injected into the tail vein of mice, which were killed 18 days later and the lungs examined. There was direct proportionality between number of viable cells injected and the number of resultant tumours, but several thousand cells were required to be injected in order to produce one tumour.

The same tumour was then grafted subcutaneously into mice, two different sizes of graft being used, and the mice were killed after various periods. The volume of the primary tumour was measured and the lung metastases counted. It was found that the number of lung metastases was positively correlated with both the size of the original graft and the duration of its growth, but not with the final size attained by the tumour. *M. H. Salaman*

2345. **The Virus-induced Papilloma-to-Carcinoma Sequence. I. The Growth Pattern in Natural and Experimental Infections**
J. T. Syverton, H. E. Dascomb, J. Koomen, E. B. Wells, and G. P. Berry. *Cancer Research* [*Cancer Res.*] **10**, 379–384, June, 1950. 25 refs.

The authors kept under observation, for periods ranging from several months to several years, 207 cottontail rabbits bearing Shope papillomata when caught and 94 cottontail and 293 domestic rabbits experimentally infected with Shope papilloma virus. The progress of

the disease is described as passing through three phases: (1) a proliferative phase, in which focal multiplication of the germinal layer of the epithelium gives rise to a "vesiculoid" eruption after 7 to 42 days, followed by extension laterally and outwards and the development of papillomatosis; these lesions may be discrete or confluent, according to the concentration of the inoculum; (2) a stationary phase; and (3) an involutionary phase, in which abnormal proliferation ceases and the lesions regress; during this phase focal transformation of the papillomatous lesion to anaplastic epithelioma occurs in a proportion of animals.

The critical period for the appearance of malignancy was at about the 12th month in cottontails and the 9th month in domestic rabbits, and malignant change occurred in about 25% of the former and 75% of the latter bearing papillomata for more than 6 months. It appeared doubtful whether the mode of infection of cottontails affected the incidence of regression or malignancy. *M. H. Salaman*

2346 **The Effect of Human Influenza Virus (Type A) on the Incidence of Lung Tumors in Mice**
P. E. Steiner and C. G. Loosli. *Cancer Research* [*Cancer Res.*] **10**, 385–392, June, 1950. 16 figs., 9 refs.

This investigation was suggested by the fact that infection with influenza virus is often followed, both in man and in the mouse, by hyperplasia of the bronchial and bronchiolar epithelium. Mice of two inbred strains—strain A with a high incidence, and C57 black with a low incidence of spontaneous lung tumours—were exposed to a mist containing human influenza virus (type A, PR–8 strain). Infection occurred in almost 100%, as judged by sample necropsies. Of the C57 mice 6%, and of the strain-A mice 14% and 53% respectively in two experiments, died between the 8th and 14th day, none dying later. Many of the survivors appeared normal, but some showed dyspnoea or asymmetry of the thorax. On naked-eye and microscopical examination the lesions in the lungs were similar to those previously described in the post-influenzal state, and 2 to 4 weeks after infection areas of epithelial proliferation were seen which were often hard to distinguish from neoplasms. Later these atrophied, sometimes leaving areas of atelectasis, fibrosis, and cyst formation; these changes persisted throughout life. No increase in the incidence of lung tumours followed influenzal infection in either strain. No tumours at all occurred in either infected or control C57 mice. In the mice of strain A, influenzal infection was judged to be non-carcinogenic on the following grounds: (*a*) there was no increase following infection in the number of mice developing tumours, or in the average number of tumours per tumour-bearing mouse; (*b*) tumours arose no more often from old influenzal lesions than from apparently normal areas; and (*c*) there was no microscopical evidence that post-influenzal epithelial hyperplasia ever progressed to tumour formation. There was a suggestion, probably not significant, that the virus may have been slightly anti-carcinogenic.
M. H. Salaman

2347. **A New Method for Bone Marrow Culture.** [In English]
C. M. Plum. *Sang* [*Sang*] **21**, 452–454, 1950. 3 figs.

A new method of marrow culture is described, in which the anterior chamber of the guinea-pig's eye is used. The marrow specimen, suspended in Locke solution containing 2% of the patient's own serum, is centrifuged; the upper layer of immature cells is then removed (mature cells accelerate fibroblast production and must be carefully excluded) and diluted with Locke solution to a volume of 0·5 ml. Of this suspension 0·05 ml. is injected by a very fine needle through the corneo-scleral junction; at the end of the culture period the entire contents of the anterior chamber are similarly removed, and smears made and stained in the usual manner.
H. McC. Giles

2348. **Investigations on the Role of Plasma Cells as Antibody Producers.** [In English]
H. Gormsen. *Sang* [*Sang*] **21**, 483–486, 1950. 8 refs.

The existing evidence for the globulin-forming function of plasma cells is briefly indicated. In a study of sternal marrow from 800 patients with diseases other than multiple myelomatosis the author found that a plasma cell count of more than 5% was invariably accompanied by hyperglobulinaemia. In patients with a serum globulin level of more than 3·5 g. per 100 ml. the converse was almost always true. Earlier work showed that rabbits hyperimmunized with polyvalent pneumococcal vaccine responded with an intense generalized plasma-cell proliferation. The antibody content of tissue extracts was related to the number of plasma cells in the tissue. "Stilbamidine", although producing specific myeloma cell inclusions in patients with myelomatosis, did not apparently interfere with antibody formation in experimental animals. *H. McC. Giles*

2349. **Agranulocytosis and Panmyelopathy Experimentally Produced by Urethane in the Cat.** (Agranulocytose et panmyélopathie expérimentales à l'uréthane chez le chat)
S. Moeschlin and A. Bodmer. *Sang* [*Sang*] **21**, 515–516, 1950.

In this paper the authors, from the University Medical Clinic, Zurich, give a preliminary account of bone-marrow changes found in 7 urethane-treated cats, 3 others being kept as controls. Cats were found to be comparatively sensitive to urethane, and repeated doses of 0·05 to 0·1 g. per kg. body weight regularly caused a severe panmyelopathy. Smaller doses retarded maturation, first of granulocytes and then of platelets, but erythropoiesis was much less affected. With increasing doses mitosis was depressed and its pattern distorted, and the marrow became diffusely hypoplastic. In general, granulocytes showed greatest sensitivity, followed by lymphocytes, megakaryocytes, and erythroblasts; eosinophils seemed peculiarly resistant, and in aplastic marrow were sometimes the only members of the white cell series. Plasma cells were relatively insensitive and even increased in numbers during the agranulocytic phase.

These changes were spontaneously reversible if urethane administration was stopped early enough; injection of large doses of folic acid and pyridoxine had no therapeutic effect. Experiments are in progress to discover whether the activity of urethane can be abolished by large doses of other substances; it is hoped that more knowledge will thus be obtained about its mode of action. *H. McC. Giles*

2350. **Experimental Macrocytic Anaemia in the Rat.** [In English]
C. M. PLUM. *Sang* [*Sang*] **21**, 437–451, 1950. 8 figs., 29 refs.

Working at the University of Copenhagen, the author found that excision of the caecum in male albino rats kept on a diet free from green vegetables was almost always followed by anaemia; in 25% this was hypochromic and responded to iron, in 40% macrocytic, with marked anisocytosis, and in the remainder normochromic. Marrow smears obtained by tibial puncture showed a normal picture except in cases of macrocytic anaemia, when there was often an increase in pro-erythroblasts and basophil erythroblasts, and a few cells were seen corresponding exactly to the megaloblasts of human pernicious anaemia. In this group 90 animals were given 0·2 or 0·3 ml. of one of two commercial liver extracts, or a 1 in 10 dilution of the same extracts, by subcutaneous injection. A reticulocyte crisis, followed by a rise in haemoglobin value and erythrocyte count, occurred in numbers ranging from 14 out of 20 to 4 out of 20, according to the dose, dilution, and preparation used. Although intestinal strictures or extensive sepsis were present at necropsy in some of the refractory cases, no cause for failure of therapeutic response could be found in the majority. *p*-Aminobenzoic and *p*-aminobenzoylglutamic acids, used in the synthesis of folic acid, were given in single or repeated doses of 0·5 mg., orally or by injection; anaemia was not affected, but both substances provoked a leucocytosis when given by injection. Two preparations of folic acid were also tested in doses of 0·5 mg.; a reticulocyte crisis occurred in 4 out of 25 and in none out of 25 after oral administration and in 10 and 6 after injection. Again no explanation could be found for most of the failures. With one preparation, a leucocytosis was noted in the 19 refractory cases among the injected group; it is suggested that this product may contain small amounts of *p*-aminobenzoylglutamic acid. *H. McC. Giles*

MORBID ANATOMY

2351. **Pleural Mesothelioma**
W. N. CAMPBELL. *American Journal of Pathology* [*Amer. J. Path.*] **26**, 473–487, May, 1950. 4 figs., 19 refs.

There has been extreme reluctance on the part of pathologists to diagnose pleural mesothelioma or even to acknowledge its existence. When it has been encountered there has always been a tendency to ascribe any pulmonary invasion to extension in a reverse direction. So deeply ingrained is this attitude that a bronchial origin is generally postulated even when no point of infiltration can be found. Bronchial carcinoma may simulate this neoplasm, but pleural mesothelioma is a real entity. The tumour is not common and no author has previously described more than 2 cases from one institution. Saccone and Coblenz (1943), however, found 200 reported cases and about 18 have been described in the American literature since. The author reports 4 cases (from 3,533 necropsies during 8 years). He claims that histologically carcinomatous areas are seen, with spaces lined by a single layer of oxyphil cells; areas composed of spindle cells are also present. The diagnosis can be made by biopsy, and the condition may be amenable to modern surgical treatment. It shows little tendency to spread. [Those who have any further doubt about the possibility of mesothelial neoplasia should read the paper by Crome (*J. Path. Bact.*, 1950, **62**, 61; *Abstracts of World Medicine*, 1950, **8**, 251).] *D. M. Pryce*

2352. **Morbid Anatomy of Tuberculous Meningitis after Chemotherapy with Streptomycin, "TB IV", and "BI 76 Tbc".** (Pathologisch-anatomische Befunde bei Leptomeningitis tuberculosa nach klinischer Behandlung mit chemotherapeutischen Mitteln (Streptomycin, TB IV and BI 76 Tbc)
C. KRAUSPE. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] **61**, 386–397, 1950. 6 figs., 25 refs.

Histological studies on a case of tuberculous meningitis ineffectively treated by a proprietary remedy and another treated with streptomycin intrathecally together with "TB IV" for 41 days confirmed findings reported by other investigators. No new, hitherto unknown, histological processes result from the influence of effective chemotherapy. The healing processes observed are due to the more protracted course of the disease, and have been found in the past on rare occasions in more chronic cases, or in the very rare cases of spontaneous healing of tuberculous meningitis. The vascular changes in the leptomeninges are discussed at length and their interpretation is attempted. The hyaline-fibrinoid necrosis of vessel walls and its relation to endangiitis obliterans found in connexion with chronic tuberculous lung lesions and other disease processes are dealt with extensively. *E. Nassau*

2353. **Morbid Anatomy of Tuberculosis after Treatment with "TB I/698".** (Pathologisch-anatomische Beobachtungen bei Tuberkulose nach TB I/698-Behandlung)
W. MÜLLER and P. STÜPER. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] **61**, 398–416, 1950. 8 figs., 19 refs.

The difficulty of assessing histological changes directly attributable to the treatment of tuberculosis with thiosemicarbazone or any other chemotherapeutic agent is stressed. Regressive changes will often be found in patients treated by collapse measures or conservative treatment only. Of 10 cases treated with TB I/698 which were extensively studied, regressive changes were prominent in a large proportion. Fresh progressive lesions were, however, quite frequently encountered even

during treatment with the drug. The regressive changes appeared as fibrosed miliary and larger tubercles. Giant cells were very conspicuous and were often the only specific cells, lying embedded in fibrous tissue. Of toxic manifestations, definite serious liver damage was seen in 2 cases and possible minor damage in others, while signs of an increased tendency to bleeding were seen on the periphery of caseous foci; in fact, 2 of the patients died of haemorrhage. A final assessment of the effect of thiosemicarbazone on tissue appearances will not be possible until a much larger material has been studied.

E. Nassau

2354. **The Morbid Anatomy of Tuberculosis in Old Age.** (Considérations anatomo-pathologiques sur la tuberculose sénile)
F. ROULET. *Annales de Médecine* [*Ann. Méd.*] **51**, 69–82, 1950. 7 figs., 12 refs.

This work is based on the findings in 270 necropsies carried out at the University of Basle on subjects over 60 years old, at which frank evidence of tuberculosis was present, although it was the cause of death in only 90 cases. The active focus was found in 245 cases around an old calcified or ossified nodule in the tracheo-bronchial lymph nodes; in fact, the lesions closely resembled the Ghon lesion and were often the size of an egg. Careful examination of the lungs in these cases failed to reveal any active primary focus, though an old, calcified, inactive lesion was often discovered. It would appear that active tuberculosis in old age is frequently caused by reactivation of an old lesion in the lymph nodes around the bifurcation of the trachea, and the author believes that this is due to the resurrection of dormant tubercle bacilli in the old focus. This reactivation may be related to the chronic inflammation of the lower trachea and main bronchi which is extremely common in old people. Tuberculosis of the tracheo-bronchial nodes frequently leads to complications: of the 245 cases of tracheo-bronchial-node infection, there was also frank tuberculous infection of the lungs in 35: in 12 cases there was a generalized haematogenous spread either from a focus in the tracheo-bronchial nodes or from an alternative site of active infection; in 13 cases there were foci both in the tracheo-bronchial nodes and elsewhere, but no generalized spread; and in 25 cases haematogenous spread had occurred, with tracheo-bronchial nodes as the only possible primary source. In the remaining 160 cases in this group the infection was confined to the tracheo-bronchial nodes.

Speaking generally, miliary tuberculosis develops more rapidly in the old than at other ages. The appearances are classical, though the tubercles may be rather large—as big as a pea or a hazel nut. In the whole series there were 16 cases of miliary spread amongst the 43 cases of frank pulmonary tuberculosis. Tuberculosis of the serous cavities is not uncommon in the elderly. Pulmonary tuberculosis may be of the chronic, apical, fibro-caseous type with cavities, or of the ulcerative, caseous type of acute tuberculosis, the frequent occurrence of which in old people may possibly be due to reduced general resistance and antibody response.

Peter Harvey

2355. **Thoracic Venous Anomalies**
J. E. EDWARDS and J. W. DUSHANE. *Archives of Pathology* [*Arch. Path.*] **49**, 517–537, May, 1950. 20 figs., 22 refs.

The authors describe 2 very rare cases of intrathoracic venous anomaly and discuss in great detail the developmental basis of the malformations found. In the first case congenital mitral atresia was combined with premature closure of the foramen ovale together with multiple small perforations of the lower part of the ventricular septum. The only exit from the left auricle was an anomalous vein, termed by the authors a "laevoatrio-cardinal" vein, which entered the left innominate vein and so allowed blood to reach the superior vena cava and right auricle. Ordinarily in mitral atresia there exists a patent foramen ovale and either a high ventricular septal defect, or absence of the ventricular septum. Mixture of venous and oxygenated blood takes place in the right auricle, and the heart—as also in the case described—is functionally biloculate.

In the second case none of the pulmonary veins entered the left auricle. They were united to form a common trunk which entered the abdomen and terminated in the ductus venosus. Oxygenated blood could reach the heart only by the left hepatic vein, inferior vena cava, and through a patent foramen ovale into the left auricle.

Both infants had been cyanosed since birth and survival was brief—4 weeks in the first case and 9 days in the second.

James W. Brown

2356. **Mixed Tumors of the Thymus. Criteria for Their Differentiation and Their Radiotherapeutic Response**
S. J. EISENBERG and P. F. SAHYOUN. *Archives of Pathology* [*Arch. Path.*] **49**, 404–417, April, 1950. 7 figs., 13 refs.

The thymus has a dual origin, branchial and mesenchymal, and its tumours usually contain both elements, though in most cases either epithelium or lymphoid tissue predominates. In the intermediate mixed grade differentiation from Hodgkin's disease may be very difficult, and the authors believe that some cases given the diagnosis of Hodgkin's disease are in fact cases of disseminated thymomata. They present a series of 7 cases, in all but one of which cervical lymph node enlargement was the principal symptom and in several of which biopsy specimens had been first reported as specimens of Hodgkin's disease, but in all of which a mediastinal mass was present. The histological criteria relied on are: (*a*) the fibrosis is of a concentric type, with formation of abortive Hassall's corpuscles; (*b*) the multinucleate giant cells are three to four times the size of those of Hodgkin's disease; (*c*) the reticulo-epithelial cells of the thymomata are better demarcated; and (*d*) their nuclei have coarser chromatin and larger nucleoli. The cases were all of longer duration than the average (37 months) for the authors' series of cases of Hodgkin's disease; they responded well to irradiation and poorly to nitrogen mustard administration. [It is probable that most pathologists would find considerable difficulty in applying the criteria suggested.]

Bernard Lennox

2357. **Pathological Changes due to Urethane in Leukaemias, Malignant Tumours of the Lymphatic System, and Hodgkin's Disease.** (Die Morphologie der Urethanwirkung bei Leukämien, malignen Tumoren des lymphatischen Systems und der Lymphogranulomatose) K. LENNERT. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] **61**, 339–370, 1950. 3 figs., bibliography.

The pathological changes brought about by urethane treatment in cases of myeloid leukaemia, acute leukaemia, lymphoid leukaemia, tumours of the lymphatic system, and Hodgkin's disease were studied in post-mortem and biopsy material from 20 subjects who had received such treatment.

In cases of chronic myeloid leukaemia there was marked reduction in extramedullary myelopoiesis, particularly in the liver, while the bone marrow was little affected. In acute leukaemia no influence on the disease process could be observed. In chronic lymphoid leukaemia regression of the lymphomata, with replacement of the lymphoid cells by a very vascular granulation tissue and eventually by hyaline material, was seen. Similar changes were observed in lymphosarcoma. In Hodgkin's disease no marked change in the histological picture was seen, apart from increased hyaline changes in the affected lymph nodes.

The site of action of urethane is believed to be the nucleus of the diseased cell, where it causes vacuolar swelling and to a lesser extent pyknosis, with the formation of giant cells. The histological changes seen after the administration of urethane strongly resemble those seen after *x*-ray treatment. Minor side-effects of urethane treatment are a reduction of lymphatic tissue and stimulation of erythropoiesis in some cases, while the more important complications are panmyelophthisis and impairment of resistance to infections, including tuberculosis. *E. Nassau*

2358. **Evidence for an Inflammatory Basis of Coronary Arteriosclerosis in the Young**
O. SAPHIR and I. GORE. *Archives of Pathology* [*Arch. Path.*] **49**, 418–426, April, 1950. 2 figs., 18 refs.

Among the many remarkable series which the files of the American Army Institute of Pathology have yielded, there is one published by Yater *et al.* (*Amer. Heart J.*, 1948, **36**, 334, 481, 483), of 866 cases of arteriosclerosis in males aged 18 to 39 years. In many of these the disease was limited to the coronary vessels. From these the present authors have selected 13 cases, all in patients aged 29 or less, for detailed histological study. They did this in the belief that the changes recognizable in the coronary vessels of later age groups are of a much less specific nature than is generally supposed. Arteriosclerosis is in their belief simply a vascular scarring, and the series of changes which may occur in the scarred area, though they may be modified by such factors as abnormalities of lipid metabolism, bear no necessary relation to the lesion which produced the scar. They adduce a considerable list of inflammatory conditions which are known to be capable of producing such scars. Consequently, they suppose that these relatively early cases of coronary disease are the most likely to give information of their origin. No clinical details are given of the cases, except that all patients died suddenly and unexpectedly of severe coronary disease. The 13 cases fell into the following four groups: (1) In 3 cases there was no evidence of inflammation. The lesions were limited to the large arteries, and consisted of eccentric intimal plaques of hyaline fibrous tissue, with varying amounts of fat. (2) In 4 cases the lesions were limited to the large arteries and similar to those of group 1, with the addition of adventitial fibrosis and cell infiltrations, and changes in the vasa vasorum, suggesting recent inflammation. (3) In 3 cases the coronary trunks were normal, but the lesions of healed or healing arteritis were present in the smaller branches within the myocardium. (4) In 3 cases the lesions of groups 2 and 3 were combined. The similarity of the lesions of smaller arteries seen in 6 cases to those of rheumatic arteritis suggests a possible rheumatic aetiology, but even minimal other evidence of rheumatism was present in only 2 cases. Otherwise, the origin of the inflammatory lesions remains a matter for speculation.

Bernard Lennox

2359. **Myeloid Metaplasia in the Intestinal Wall, Lymph Nodes, and Spleen in Bacillary Dysentery.** (О миэлоидной метаплазии в стенке кишечника, лимфатических узлах и селезенке при бациллярной дизентерии) M. J. SHENDEROVICH. Архив Патологии [*Arkh. Patol.*] **12**, No. 1, 89–94, 1950. 16 refs.

Myeloid metaplasia was present in the intestinal walls, and particularly in the submucosa, of 14 out of 32 subjects dying from bacillary dysentery. In 22 cases out of 28 it was present in the regional lymph nodes, and in 22 cases out of 25 in the spleen. The myeloid metaplasia in the gut was roughly proportional to the amount of coincident oedema and fibrinous exudate. *L. Crome*

2360. **A Distinctive Vacuolar Nephropathy Associated with Intestinal Disease**
J. P. KULKA, C. M. PEARSON, and S. L. ROBBINS. *American Journal of Pathology* [*Amer. J. Path.*] **26**, 349–377, May, 1950. 10 figs., 28 refs.

Among 152 cases of chronic intestinal disease (including 72 of ulcerative colitis) which gave rise to malnutrition, anaemia, hypoproteinaemia, electrolyte imbalance, and sepsis there were 15 in which highly vacuolated cells (apparently hydropic) were found in the proximal convoluted tubules of the kidney. *D. M. Pryce*

2361. **The Renal Appearances in the Microscopic Form of Periarteritis Nodosa**
J. WAINWRIGHT and J. DAVSON. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 189–196, April, 1950. 8 figs., 5 refs.

The present paper is an extension of an earlier publication (Davson, Ball, and Platt, *Quart. J. Med.*, 1948, **17**, 175) in which the authors described the renal lesions in cases of polyarteritis nodosa. They now record in detail the renal changes in 4 further cases of the disease and 2 probable cases, stressing in particular the morbid

anatomy, which they consider to be distinctive. The patients' ages were 55, 31, 41, 19, 68, and 64 respectively. Five of the 6 had a short pyrexial illness with haematuria, albuminuria, and rapidly developing uraemia, but no hypertension. The kidneys were enlarged, smooth, and congested. The cut surface showed a swollen, bulging cortex with a mottled red and yellow colour and an indistinct pattern. The characteristic feature was the presence of visible glomeruli as opaque grey spots. Microscopically the kidneys in all cases showed an "explosive" glomerulitis with necrosis, cellular infiltration, and pericapsular infiltration. Polyarteritis nodosa was found in 4 cases, but its extent varied from the involvement of many organs to that of a few arteries only.

The authors feel justified in including their 2 further cases because of this variability and because in all other respects they were exactly similar. They suggest that in middle-aged patients who die of a fulminating acute nephritis without hypertension and whose kidneys show the naked-eye lesions which they describe, a presumptive diagnosis of polyarteritis nodosa can be made in the post-mortem room. *C. V. Harrison*

2362. **Sequences in the Development of Cirrhosis of the Liver in Cases of Erythroblastosis Fetalis**
J. M. Craig. *Archives of Pathology* [*Arch. Path.*] **49**, 665–686, June, 1950. 10 figs., 23 refs.

Changes in the liver were studied in 16 cases of erythroblastosis from the Children's Medical Center and the Boston Lying-in Hospital.

In the first group of 10 cases parenchymal necrosis of the liver was found histologically, but there was no increase in the reticulum. In 9 of these there was support besides the necropsy findings for a diagnosis of erythroblastosis. The author discusses theories of the origin of parenchymal necrosis.

A second group consisted of 4 cases of obvious and significant increase in the reticulum and fibrous tissue of the liver. All 4 cases occurred before the discovery of the Rh factor but the family histories are consistent with a diagnosis of erythroblastosis, and in 3 cases there was strong corroborative evidence. The third group consisted of 2 cases of cirrhosis following erythroblastosis, in which the infant survived for 3 weeks and for one month respectively. Both livers showed considerable increase in reticulum with gross enlargement of the portal triads.

Out of 141 infants dying of erythroblastosis, only in 11% did the liver show severe anatomical damage. The incidence appears to be independent of the mother's parity, the severity of the disease, or the length of postnatal survival. Necrosis, cell regeneration, and fibrosis occur in antenatal and postnatal life. Before birth they may be due to the effect on the liver of undiluted maternal antibodies. Possibly the high intrauterine pressure at birth may enable larger molecules to cross the placental barrier. The author finds the continuation of liver damage after birth more difficult to explain. Perhaps the huge demands for oxygen by a liver concerned with increased erythropoiesis because of anaemia may be responsible, though the lesions are not typically those of anaemia or toxaemia. Hepatic damage is not a specific lesion of kernicterus.

The author is unable to explain the distribution of free iron in the Kupffer and parenchymal cells, which is not parallel to the degree of bile stasis.

Peter Harvey

2363. **Lesions of Galactose Diabetes. Pathologic Observations**
L. S. Bell, W. C. Blair, S. Lindsay, and S. J. Watson. *Archives of Pathology* [*Arch. Path.*] **49**, 393–403, April, 1950. 4 figs., 10 refs.

At necropsy on a girl dying on the eighth day of life after an illness of 2 days, the principal changes seen were in the liver, which was enlarged and showed intense fatty change and numerous focal necroses; the renal epithelium also was fatty. A brother of this patient became ill on the fifth day of life, with vomiting followed by fever, icterus, and enlargement of liver and spleen. Galactosuria and galactosaemia were demonstrated, and the elimination of milk from the diet resulted in cure. Eight days after elimination of milk a liver biopsy examination was made: it revealed an irregular lobular pattern, often pseudo-acinous, and with many mitoses, which was interpreted as due to regeneration after recent severe liver damage; fatty change was less severe than in the previous case. The glycogen content of the cells in this case was normal. The importance of these 2 cases lies in the demonstration that the enlargement of the liver is not due to glycogen storage, and that the condition is not, as has been supposed, a variant of von Gierke's disease. [By a regrettable dichotomy of publication, the clinical and biochemical findings in this case are to appear later in *J. Paediat.*] *Bernard Lennox*

2364. **Sarcoidosis of the Spleen. Report of Four Cases with a Twenty-Three Year Follow-up in One Case**
S. Kay. *American Journal of Pathology* [*Amer. J. Path.*] **26**, 427–443, May, 1950. 11 figs., 23 refs.

In the 4 cases of Boeck's sarcoid described, the preponderant lesions were in the spleen. This event is sufficiently common for the condition to be considered in the differential diagnosis of splenomegaly. The condition is identical with the splenomegaly described by Stengel-Wolbach. The author thinks that the asteroid bodies found in the giant cells in these cases may be derived from fibrinoid necrosis. They are not specific and may be found in many conditions. No Schaumann bodies were seen. *D. M. Pryce*

2365. **Clinical and Pathological Considerations Based on 1,008 Cases and 100 Necropsies on Premature Infants.** (Consideraciones clínicas y anátomopatológicas basadas en 1008 casos y 100 autopsias de prematuros)
E. Soto Pradera and F. Fuste. *Archivos Médicos de San Lorenzo* [*Arch. méd. San Lorenzo*] **1**, 16–32, Jan., 1950. 16 figs., bibliography.

The symptoms and clinical findings in a series of 1,008 cases of prematurity are analysed and the cases classified accordingly. Four main syndromes are described: respiratory, digestive, cardiovascular, and central

nervous system. Babies with respiratory and intracranial disorders tend to die in the first 48 hours of extrauterine life, while malnutrition and sepsis are not fatal for several days. In a series of 100 necropsies on premature infants lesions of the liver were found in 12%. [These cases are said to form a distinct group, but the only description of the pathology is confined to the statement that the appearances resembled those of atrophic cirrhosis.] Vascular lesions of the placenta are said to have been found which resemble those present in acute rheumatism or periarteritis nodosa. These are described as showing only the mesenchymal reactions of hypersensitivity. These findings lead the authors to suggest that some types of abortion and foetal immaturity are due to a foetal sensitization against certain maternal toxins. *George Hickie*

2366. **Carcinoma of the Head of the Pancreas. The Effects of Obstruction on the Ductal and Acinar Systems**
E. A. HAUNZ and A. H. BAGGENSTOSS. *Archives of Pathology* [*Arch. Path.*] **49**, 367–386, April, 1950. 6 figs., 16 refs.

CLINICAL PATHOLOGY

2367 (*a*). **The Thermal Coagulation Point of Blood Serum. I. Method and Clinical Interpretation**
G. B. J. GLASS. *American Journal of Medicine* [*Amer. J. Med.*] **8**, 745–754, June, 1950. 3 figs.

The principle upon which the thermal coagulation of blood serum is based is discussed and the results of 1,500 determinations of the thermal coagulation point (the minimum temperature which, acting for one minute, is sufficient to coagulate the serum) on the blood of 1,160 individuals, including 60 normal subjects, are presented. It was found that the thermal coagulation point of serum is increased in many conditions, including malignant tumours, ulcerative colitis, pyloric stenosis, prolonged obstructive jaundice, many infective diseases, extensive burns, and frostbite, and also in over 40% of pregnant women. It is concluded that determination of the thermal coagulation point of serum is a readily performed non-specific test of illness, the degree of abnormality following to a great extent the course of the disease. In some chronic diseases its level reflects the gravity of the lesion and it may aid in determining the probable survival time. *L. A. Elson*

2367 (*b*). **The Thermal Coagulation Point of Blood Serum. II. Significance of the Principle of Defective Thermal Coagulation for Diagnosis of Cancer**
G. B. J. GLASS. *American Journal of Medicine* [*Amer. J. Med.*] **8**, 755–758, June, 1950. 3 figs.

The thermal coagulation point of blood serum (see Abstract 2367 (*a*)) has been determined in 162 cases of cancer. Defective thermal coagulation, as evidenced by an increase in thermal coagulation point, was found in the serum in about 70% of cases of carcinoma of the gastro-intestinal tract and of the bile passages and liver, in about 60% of cases of malignant tumours of bones, thyroid, and prostate, but in only about 20% of cases of cancer of the female genital organs, breast, skin, lip, tongue, and lungs. The test is considered to provide a non-specific index of illness, but owing to the large percentage of false-negative results (normal coagulation in cancer) and false-positive results (abnormal thermal coagulation in non-neoplastic diseases) it cannot be used for the early diagnosis of cancer in the general population. *L. A. Elson*

2367 (*c*). **The Thermal Coagulation Point of Blood Serum. III. Correlation with Serum Proteins, Sedimentation Rate and Weltmann Reaction**
G. B. J. GLASS. *American Journal of Medicine* [*Amer. J. Med.*] **8**, 759–766, June, 1950. 5 figs., 47 refs.

An attempt was made to correlate disturbances in the thermal coagulation point of blood serum (see Abstract 2367 (*a*)) with changes in the serum total protein, albumin, and globulin content, erythrocyte sedimentation rate (E.S.R.), and Weltmann heat-flocculation reaction (Weltmann, *Med. Klinik*, 1930, **26**, 240) in patients with malignant and non-malignant diseases as compared with normal subjects. It was found that the thermal coagulation point of the serum bears no direct relation to the E.S.R. or to the result of the Weltmann test. Abnormal thermal coagulation of blood serum appears to depend upon quantitative, and perhaps also qualitative, disturbances in serum albumin level, although the possibility that additional factors, such as α- and β-globulin levels, are also involved cannot yet be excluded. *L. A. Elson*

2368. **Defective Thermal Coagulation of Blood Serum in Cancer and Other Diseases and its Clinical Interpretation**
G. B. J. GLASS. *Journal of the Mount Sinai Hospital* [*J. Mt. Sinai Hosp.*] **17**, 1–20, May–June, 1950. 6 figs., 43 refs.

The physico-chemical basis of the thermal coagulation of blood serum is considered and a brief history is given of the development of thermal-coagulation tests. The incidence of defective thermal coagulation of serum in disease differs from that of most of the other non-specific serological reactions, and the test gives information which cannot be obtained by studying the erythrocyte sedimentation rate, protein content of the serum, or various flocculation reactions. It may therefore prove useful as a diagnostic and prognostic aid, in association with other clinical and laboratory data.

The technique of assessing defective thermal coagulation by determination of the thermal coagulation point of serum is considered simpler than measurement of the iodoacetate index by the Huggins method; the information obtained is similar in significance and serves as a very useful but entirely non-specific index of serious organic illness. It has a limited diagnostic value in some types of malignant disease, but cannot be applied to the general diagnosis of cancer, or used as a screening test for early cancer cases among the population because of the high incidence of false-negative and false-positive results. *L. A. Elson*

2369. **Alkaline Phosphatase Activity of Human Serum in Cancer**
A. BERNHARD and L. ROSENBLOOM. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 164–167, May, 1950. 13 refs.

In an investigation of the alkaline-phosphatase activity of the blood in cases of cancer and of non-cancerous disease, the serum of the vast majority of non-cancerous individuals, including pregnant women, showed normal dephosphorylation. The chief exceptions were in cases of diseases of the liver and pancreas (mostly with jaundice) and those of endocrine disturbances, particularly thyroid disease. In the presence of malignancy, phosphorus release of the serum was generally higher. The highest values were found in the blood of patients with tumours of the liver, pancreas, or genito-urinary system. In over 92% of all the patients from whom a malignant tumour had been excised, and who were symptom-free, the dephosphorylation by the serum of the various substrates employed was within normal limits. *R. J. Ludford*

2370. **A Clinical Study of the Iodoacetate Index (Huggins Test) in Cancer and in Various Nonmalignant Pathologic Conditions**
D. R. GILLIGAN, J. T. ROTHWELL, and S. WARREN. *New England Journal of Medicine* [*New Engl. J. Med.*] **242**, 807–813, May 25, 1950. 2 figs., 15 refs.

The iodoacetate index as related to the total protein concentration of the serum (Huggins *et al.*, *Cancer Res.*, 1949, **9**, 177) has been determined in over 200 cases, including normal subjects, patients with cancer, and patients with various non-malignant pathological conditions. Of the cancer patients in 72% the iodoacetate index was below normal, but in 28% of cases, including many with extensive carcinomatous lesions and some with metastases, normal values were obtained. In 42% of patients with various non-malignant pathological conditions (mainly infectious diseases, ulcerative lesions, inflammatory processes, or necrotic changes) low values similar to those in cancer patients were obtained, and major surgical operations were often found to reduce the index.

It is concluded that the index does yield useful information concerning a systemic effect of certain cancers in human beings, but does not constitute a useful tool for the diagnosis of the presence of cancer. *L. A. Elson*

2371. **The Distribution of Bone Marrow in the Human Sternum**
J. DENST and R. M. MULLIGAN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 610–613, July, 1950. 11 refs.

2372. **The Clinical Significance of Sodium and Potassium Analyses of Biological Fluids: Their Estimation by Flame Spectrophotometry**
V. WYNN, S. SIMON, R. J. H. MORRIS, I. R. MCDONALD, and D. A. DENTON. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 821–835, June 24, 1950. 11 figs., bibliography.

2373. **The Protein-bound Calcium Content of the Serum and its Physiological and Pathological Variations.** (Calcium protéique du sérum et ses variations physiopathologiques)
M. HOCHFELD and J. HOCHFELD-OLLIVIERO. *Presse Médicale* [*Pr. méd.*] **58**, 586–588, May 27, 1950. 3 figs., 15 refs.

The authors estimated the protein-bound and total calcium content of serum, obtaining results for diffusible calcium by difference, in ox blood and in the blood of 30 patients suffering from various disorders. They used a new technique of estimation, in which they precipitated the serum proteins with acetone–alcohol at a fixed temperature and *p*H, and washed the precipitate with organic solvents at low temperature and a fixed *p*H to remove all the protein-bound calcium. Full technical details are to be published elsewhere. Results give good agreement with those obtained by the ultrafiltration method. Comparison of the new method with the McLean–Hastings method in 30 patients with various disorders showed a much greater variability in values for diffusible calcium in the new than in the older method. Treatment with stilboestrol reduced the amount of protein-bound calcium and caused the amount of diffusible calcium to increase, while methyltestosterone treatment caused the protein-bound calcium level to rise, but had little effect on the diffusible fraction. Injections of calcium gluconate increased both fractions equally. In one case of chronic tetany a low diffusible calcium level was not increased by treatment with oestradiol benzoate. Estimations, made hourly in cases of Paget's disease after intravenous injections of sodium citrate, showed a slight fall of diffusible calcium value and an increase in protein-bound calcium content, the same effect being obtained when sodium citrate was given in this way to patients with tetany and arteriosclerosis. In all cases treated with citrate the total calcium content was increased.
Walter H. H. Merivale

2374. **Correlation Between Electrophoretic and Chemical Partitions of Serum Proteins**
H. POPPER, J. DE LA HUERGA, M. FRANKLIN, W. B. BEAN, W. D. PAUL, J. I. ROUTH, and F. SCHAFFNER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 530–538, June, 1950. 7 figs., 19 refs.

2375. **An Accurate Method for Glucose Determination**
J. L. POPE. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 801–805, Sept., 1950. 6 refs.

2376. **Sham Feeding as a Test for Gastric Function**
O. NORING. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **2**, 120–124, 1950. 12 figs., 7 refs.

The most common method of studying the cephalic phase of gastric secretion clinically is by the insulin test. Sham feeding is much used in animal experiments, however, and this is an account of its application to ambulatory patients. The patients came to the laboratory in the morning fasting. A fine-calibre duodenal

tube was introduced through the nose into the stomach, which was emptied then and after a further 10 minutes. The patients then chewed 2 to 3 buttered black-bread sandwiches made with various sandwich spreads, for 10 minutes. Swallowing was avoided. The gastric secretion was measured in every 10th minute for 40 to 50 minutes. The samples were examined for rate of secretion, acidity (Congo red and phenolphthalein), total chloride, and pepsin.

In those cases in which the vagus nerves were intact, sham feeding caused a marked increase in the amount of gastric secretion and in its chloride and pepsin content. The rate of secretion was higher in patients with peptic ulcer. The sham feeding does not involve any discomfort or risk and it provides a more physiological type of stimulus than the insulin test. The test affords a satisfactory picture of the cephalic phase of gastric secretion and is recommended when it is necessary to decide whether vagotomy has been complete.

Malcolm Woodbine

2377. **Determination of Gastric Acidity without Intubation by Use of Cation Exchange Indicator Compounds**
H. L. SEGAL, L. L. MILLER, and J. J. MORTON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 218–220, May, 1950. 2 refs.

A cation exchange indicator compound is described in which the cation is quinine, this being displaced by hydrogen cations of dilute hydrochloric acid or gastric juice, only slightly by sodium, potassium, and calcium, but appreciably by magnesium. This compound may be used in determining gastric acidity by the photofluorimetric estimation of the quinine excreted in the urine following its oral administration. Of 38 patients known to have free hydrochloric acid in the gastric juice, 34 excreted quinine in the urine during the first hour after administration, whereas 20 of 25 patients with achlorhydria excreted none before the third hour.

F. W. Chattaway

2378. **Some Features of Pathological Physiology of the Pancreas in Chronic Gall-bladder Disease.** (Algunos aspectos fisiopatologicos de las alteraciones del pancreas en las colecistopatias cronicas)
D. URRUTIA, J. MARTINI, S. GRINSCHPUN, V. ARAYA, O. GONZALEZ, and E. DE GUZMAN. *Revista Médica de Chile* [*Rev. méd. Chile*] **78**, 245–258, April, 1950. 12 figs., bibliography.

The authors stress the difficulty of investigating diseases of the pancreas in spite of numerous clinico-pathological tests. They review the history of the physiology of the pancreas and then enumerate the methods used for estimating its function. Amongst these are the following: (1) Stimulation of the external secretion of the pancreas by secretin. The fluid is obtained by duodenal intubation, and the concentration in it of the various enzymes is then estimated. (2) Stimulation of the vagus by cholinergic drugs. (3) Analysis of the pancreatic juice obtained by duodenal intubation alone. (4) Estimation of pancreatic enzymes (mainly lipase and amylase) in the blood. (5) Estimation of the enzyme content of urine. This is not so reliable as estimation in serum. (6) Examination of the faeces for fats and undigested proteins. (7) Study of changes in carbohydrate metabolism.

Several of the above methods were then applied to 75 cases of cholelithiasis, confirmed by radiology and operation. In 75% of these cases the amount of pancreatic juice obtained by duodenal intubation was reduced. Serum lipase estimation is unreliable except in acute cases, when it may be used to gauge progress. Determination of sugar and cholesterol values in blood is of secondary importance. In the faeces, pathological values are found only when the disease process is well advanced; the authors stress the need for a suitable preliminary diet. Palpating the pancreas at laparotomy is of little value, and biopsy is somewhat dangerous. The pancreas itself cannot be investigated radiologically except in cases of carcinoma of the head, which causes widening of the duodenal loop, and in cases of pancreatic calculi. In their final analysis the authors regard duodenal intubation and serum lipase determination as the most valuable tests.

Paul B. Woolley

2379. **Diagnosis of Lipoid Pneumonia by Examination of Sputum**
S. LOSNER, B. W. VOLK, W. R. SLADE, L. NATHANSON, and M. JACOBI. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 539–545, June, 1950. 4 figs., 17 refs.

From each of 20 patients in whom the diagnosis of lipoid pneumonia was suspected on clinical or radiological grounds, three to five consecutive 24-hour specimens of sputum were collected; sputum from a control group of 45 patients was also examined. All patients were placed on a fat-free diet for 4 days before, and during the period of, the investigation. Six smears were made from each specimen, the more watery specimens being first centrifuged; three of the smears were stained with Sudan IV and haematoxylin and the rest with a modified Wright's stain. The presence of stainable fat in the vacuoles of macrophages, or of " abundant " extracellular fatty material, was taken to denote a positive result.

Lipoid material was found in the sputum of 19 of the 20 patients suspected of having lipoid pneumonia, and of 2 of the control group. Needle aspiration of the lung and examination of the material obtained confirmed the diagnosis in 20 of these 21 patients. Most of them were suffering from diseases of the nervous system or rheumatoid arthritis and all but 2 had taken mineral oil or nasal drops continuously or occasionally over periods ranging from 2 to 30 years. [It is a pity that no details are given for the control group. There must be few people over middle age who have not at some time or other taken mineral oil or oily nasal drops.] In 5 cases there were no respiratory symptoms, but a diagnosis of lipoid pneumonia had been made on routine *x*-ray examination of the chest; the remainder had productive coughs. The positive sputum findings were intermittent in a few cases; in one case diagnosed radiologically, the first four sputum examinations proved negative.

A. Michael Davies

Microbiology

2380. **A Possible Mode of Transfer of Infection by Syringes used for Mass Inoculation**
R. J. EVANS and E. T. C. SPOONER. *British Medical Journal* [*Brit. med. J.*] **2**, 185–188, July 22, 1950. 2 figs., 14 refs.

Experiments were designed to show how infection may be transferred during mass inoculations for which a "common syringe and separate needle" technique is employed.

If 0·1 ml. sterile broth, from a sterile syringe filled with 1 ml. of the broth, was injected intraperitoneally into a mouse dying of an experimental peritonitis—induced by a highly virulent smooth strain of type-I pneumococcus—and the needle was changed and a further 0·2 ml. injected intraperitoneally into a normal mouse, the infection was carried over. Indeed it appeared from experiments of this sort that little protection against carry-over infections was conferred by changing the needle.

By using bacterial cultures in a simple but ingenious piece of apparatus called an "artificial mouse", it was possible to compare quantitatively the risk of carry-over infections with changed and unchanged needles. The difference was not great. [The records suggest that the needle was changed once only in each series. It would have been of some interest in estimating risk of carry-over infection in mass immunization to have made counts of viable organisms after second or third needle changes.] Further experiments showed that the suck-back was independent of the movement of the plunger, although of course this might be a factor. The possibility that increased pressure in the tissues round the needle point aided transfer was similarly disposed of; it was sufficient to submerge the tip of the needle below the surface of infected fluid for the syringe to be infected when the needle was removed. It would appear clear, therefore, that the negative pressure created by pulling off the needle when its lumen contains fluid was sufficient to suck that fluid up into the shoulder of the syringe.

The authors conclude that, although the risk of carrying over bacterial infection during mass immunization is small, it does exist when the "common syringe and changed needle" technique is employed; yet since the experiments showed that infection is not always carried over, this procedure must be safer than that of not changing the needle. However, when virus infections such as viral hepatitis have to be considered, the risk may well be greater. [Rubber-capped multiple containers, where replacement-air is commonly injected before withdrawal of the prophylactic, can be also infected by this means. A resistant organism may actually grow and multiply under certain conditions in the prophylactic, and should a half-used container be subsequently used after some days' interval the danger in mass immunization can be very real. This fact should always be borne in mind when multiple containers are used.]

H. J. Bensted

2381. **Use of Ultraviolet Light and Fluorescent Dyes in Bacterial Counting**
L. W. GREENE and H. C. HESSELTINE. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 171–173, May, 1950. 1 fig., 4 refs.

2382. **The Mycotic Flora of the Vagina.** (Sulla flora micotica della vagina)
F. FERRARIS and G. GAZZERA. *Minerva Ginecologica* [*Minerva ginec.*] **11**, 159–162, April, 1950. 21 refs.

VIRUSES

2383. **Some Properties of Normal Chick Allantoic Fluid in Relation to Influenza Virus Hemagglutination**
J. R. POLLEY, M. M. BURR, and A. L. GILLEN. *Canadian Journal of Research. E. Medical Sciences* [*Canad. J. Res. (E)*] **28**, 113–120, June, 1950. 12 refs.

In normal embryonated eggs incubated in a forced-draught incubator at 37·5° C. with a humidity of 80%, it was shown that, as the period of incubation increased from the 10th day onwards, the *p*H of the allantoic fluid progressively declined (7·4 to 8·2 on the 10th day; 5·2 to 6·7 on the 18th day), the *e*H remained positive, the total solid content increased, the non-specific haem-agglutinin titre remained low, and the titre of the inhibitor of influenza-virus haemagglutination increased rapidly (usually a four-fold rise from the 10th to the 18th day).

There is reason to believe that the increasing titre of inhibitor is connected with the increase in total solids and not with the fall in *p*H. It is not due to the presence of urates, because dialysis in "cellophane" bags did not affect the titre. Although the inhibitor is known to be a compound of relatively high molecular weight, it has not yet been identified.

R. Hare

2384. **The Uptake of Radioactive Phosphorus by Influenza Virus A (PR8 Strain)**
A. F. GRAHAM and L. MCCLELLAND. *Canadian Journal of Research. E. Medical Sciences* [*Canad. J. Res. (E)*] **28**, 121–134, June, 1950. 3 figs., 16 refs.

When P^{32} was injected into the allantoic sac of embryonated eggs 3 hours after their inoculation with influenza-A virus (PR8), it was incorporated into the substance of the virus. There was no evidence that direct exchange took place between virus and isotope when virus was suspended in it, nor could the isotope be removed from the virus by repeated washing after its incorporation in the course of growth.

The infectivity, sedimentation characteristics, and morphology of the purified radioactive virus were not significantly different from those of unlabelled virus, but because only one radioactive phosphorus atom was

present in every 66,500 particles of virus, it is impossible to say whether labelled virus behaves in the same way as unlabelled.

When an attempt was made to increase the yield of radioactive virus by the injection of quantities of the order of 450 to 600 microrutherfords (μrd) of P^{32}, a significant number of the embryos died. Because there was no reason to believe that this was due to toxic material in the P^{32}, it was concluded that these deaths were due to injury by β-radiation, although there was no evidence that the presence of P^{32} significantly altered the yield of virus, even when doses close to those which were lethal were administered. *R. Hare*

2385. **The Hirst Reaction ; Its Biological Interpretation in Children and Infants.** (La réaction de Hirst; son interprétation biologique chez l'enfant et le nourrisson)
G. Gateigne, C. Hannoun, R. A. Marquézy, and P. Debray. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2519–2523, July 14, 1950. 1 fig., 14 refs.

This is essentially a review of well-established methods for the culture and serological diagnosis of influenza virus, with particular reference to the haemagglutination reaction of Hirst. Some experiments are described in which the antihaemagglutinin titre of sera from newborn babies was found to correspond closely with the titre in placental blood from the mother. The serum titre of babies aged 2 to 10 months and of children aged 4 to 14 years varied from 0 to 160 and from 160 to 640 respectively.

[The authors are apparently unaware that non-specific antihaemagglutinins are common in children's serum.] *J. F. McCrea*

2386. **Cold Agglutinins. Their Clinical Significance and Biological Importance in Primary Atypical Virus Pneumonias.** (Les agglutinines froides. Leur signification clinique; leur importance biologique dans les pneumonies atypiques primitives à virus)
A. Eyquem. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2523–2531, July 14, 1950. 2 figs., 14 refs.

After a critical review of the significance of the cold-agglutinin reaction, the author stresses the need for rigid standardization of the method of estimation. In the recommended technique both serum and citrated plasma are used; they are warmed to 37° C. before the test, but are not inactivated. Fresh erythrocytes from one donor are washed at 37° C. and suspended in saline at the same temperature before being added to serial dilutions of serum and plasma. The first reading is made after 18 hours at 3° C., and the second after a further 30 minutes at room temperature. Control tests are run in parallel, the patient's own erythrocytes at 3° C. and group-O cells at 37° C. being used. The role of the cold-agglutinin test in the diagnosis of viral pneumonia is discussed. *J. F. McCrea*

2387. **Molecular Kinetic and Electrophoretic Properties of Bacteriophages**
F. W. Putnam. *Science* [*Science*] **111**, 481–488, May 5, 1950. 4 figs., 22 refs.

2388. **Bacteriophage: An Essay on Virus Reproduction**
S. E. Luria. *Science* [*Science*] **111**, 507–511, May 12, 1950. 34 refs.

BACTERIA

2389. **A New Group of Haemolytic Streptococci for which the Designation " Group O " is Proposed**
J. M. Boissard and P. J. Wormald. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 37–41, Jan., 1950. 5 refs.

During routine examinations carried out in the Public Health Laboratory Service, Cambridge, 22 strains of haemolytic streptococci were isolated which could not be assigned to any of the known groups, and for which the designation " O " is suggested. Nine strains had a similar colonial appearance, and an antiserum prepared with one of them gave precipitin reactions with the homologous strain and with 7 of the 8 other strains. In later work, over 90 strains which reacted with this serum were isolated. After 18 hours' growth on blood agar, strains of the new type form colonies with a striated margin. The surface is matt at the edge and smooth over the centre. The degree of haemolysis varies from the production of a green zone to typical β-haemolysis. In glucose-broth the organisms form a gelatinous mass which consists of chains of cocci of great length. A table of the fermentation reactions is given. Most of the strains were isolated from routine swabs of the throats of healthy persons in the Cambridge area. They were not pathogenic for mice. *D. J. Bauer*

2390. **Type-specific Agglutinins in *Corynebacterium diphtheriae* Infections**
A. A. Ferris. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 157–164, April, 1950. 9 refs.

In this investigation *Corynebacterium diphtheriae* strains from patients with clinical diphtheria or from carriers were preserved and the agglutinating effect on these strains of samples of serum collected from the same patients, on the day of admission to hospital and at weekly intervals after that until bacteriological clearance, was studied. Slide agglutination was practised, with suspensions in 5% sodium chloride of growth of *C. diphtheriae* strains on Loeffler serum slopes, doubling dilutions of serum being made by the drop method in 0·85% NaCl and equal drops of serum dilution and bacterial suspension being mixed on paraffined slides. Some sera were tested against strains stable in 0·85% NaCl and some tube-agglutination tests were carried out with sera in which 5% NaCl was used for suspensions and for serum. The former tests gave titres two to four times higher, and the latter about five times higher, than those in the routine slide-agglutination method.

In cases of acute nasopharyngeal diphtheria agglutinins began to appear in the third week and reached their maximum titre during the fifth week. The agglutinins persisted as long as the bacteria remained in the nasopharynx. The agglutinins were specific for the serological subtype of the *C. diphtheriae* type strain

responsible for the infection. The titres ranged from 1 in 2 to 1 in 256. Cross-reactions, if present, were of considerably lower titre. Two serological subtypes of the gravis, 2 of the intermedius, and 4 of the mitis type were identified and some of them could be correlated with Hewitt's serological subtypes. Homologous agglutinin titres were present in over 50% of symptomless carriers. The author succeeded in demonstrating the appearance of the corresponding agglutinins in 2 cases of cross-infection in the ward.

It was also shown conclusively that agglutinins heterologous to the type present were residual agglutinins of an earlier and subclinical infection with another type. Penicillin therapy, by freeing the patients sooner of bacteria, tended to depress the agglutinin titres.

The observations may be of importance in the question of antibacterial immunity in diphtheria.

K. S. Zinnemann

2391. **Factor from the Respiratory Tract of Man Capable of Inhibiting the Growth of *Corynebacterium diphtheriae***
M. Arvidson, H. Ericsson, O. Ouchterlony, and B. Vahlquist. *Acta Pathologica et Microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **27**, 263–269, 1950. 23 refs.

In spite of the large number of infected persons who entered Sweden during the second world war the incidence of diphtheria in that country increased only moderately as compared with other countries in north-west Europe. The authors studied the conditions on the surface of mucous membranes having an inhibiting effect on the development of *Corynebacterium diphtheriae*. Dold and Weigmann (*Z. Hyg. InfectKr.*, 1934, **158**, 116) reported the existence of an inhibitory factor in human saliva and the authors decided to re-examine the effect of saliva. The technique chosen consisted in: (1) incubating equal quantities of saliva and 24-hour broth cultures of *C. diphtheriae* for 20 hours at 37° C. and determining by subculture whether inhibition had taken place; (2) testing the inhibitory effect by the cup method used in antibiotic activity tests; and (3) testing the pharyngeal flora of normal persons for an antagonistic effect to *C. diphtheriae*. In each test a gravis strain and virulent and avirulent mitis strains were used.

Method (1) gave negative results with the saliva of all 15 persons tested. In method (2) the saliva of 10 subjects tested in 90 cups against three different strains of *C. diphtheriae* showed an inhibition zone in 68 cups. From all cups surrounded by an inhibition zone α-haemolytic streptococci were cultured. By method (3) it was found that only certain colonies of the flora of 11 out of 14 individuals had an inhibitory effect on *C. diphtheriae*. On isolation and identification the colonies exerting an inhibitory effect were found to be α-haemolytic streptococci of the *Streptococcus salivarius* type. When pure strains from the pharyngeal flora were examined it was found that 13 different strains of α-haemolytic streptococci produced inhibition of *C. diphtheriae*, whereas 16 strains of β-haemolytic and 9 of α-haemolytic streptococci, 12 strains of *Staphylococcus aureus*, and 14 of *Staph. albus* strains had no such effect. Filtrates of cultures of α-haemolytic streptococci, obtained by means of an Elford filter, were found to inhibit *C. diphtheriae*. The active substance did not pass through a Seitz filter. The inhibitory effect of α-haemolytic streptococci was most marked on nutritionally deficient media. A basic medium containing 50% of the normal peptone and meat-infusion content was used for further experiments, in which it was found that inhibition could be prevented by the addition of 10% horse or sheep blood, but not by 10% horse serum, either normal or after heating to 56° C. or 100° C.

Examination of swabs from cases of diphtheria produced no conclusive evidence of the antagonistic action of α-haemolytic streptococci. In 18 out of 106 positive swabs both *C. diphtheriae* and α-haemolytic streptococci were present and all the α-haemolytic streptococci inhibited the strains of *C. diphtheriae* isolated.

K. S. Zinnemann

2392. **A Direct Method for the Determination of the Sensitivity of Tubercle Bacilli to Streptomycin**
G. P. Youmans, A. Ibrahim, J. Sweany, and H. C. Sweany. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **61**, 569–577, April, 1950. 2 figs., 3 refs.

2393. **Plate Method for the Determination of Streptomycin Sensitivities of *Mycobacterium tuberculosis***
B. H. Johnson. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **61**, 578–581, April, 1950. 7 refs.

IMMUNITY

2394. **A Skin Test for Infectious Hepatitis**
G. Henle, M. Drake, W. Henle, and J. Stokes. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. N.Y.*] **73**, 603–605, April, 1950. 2 refs.

After 10 passages in chick embryo tissue culture, the Akiba strain of infective hepatitis virus was passaged four times at 37° C. for periods of 7 days each in the amniotic cavity of 8-day-old chick embryos. After two or three further passages of 5 days each, the virus was collected as amniotic fluid and inactivated by exposure to ultraviolet light for a period five times longer than that required to inactivate influenza virus. After adequate tests for sterility and absence of living virus, the inactivated material was used as skin-test antigen on persons who had suffered from infective hepatitis or had been exposed to it, and on persons who had suffered from serum hepatitis. A positive result (defined as the appearance within 24 hours of intradermal injection of an indurated area of somewhat brownish erythema 4 to 45 mm. in diameter, persisting though in diminished intensity for up to a week) was obtained in all 24 persons exposed to infective hepatitis virus who had developed symptoms, except one who also gave a reaction with the control fluid—amniotic fluid into which saline had been injected instead of virus. The reactions with the control fluid were generally smaller and not indurated, and faded sooner than those after injection of inactivated virus. Of 8 persons exposed to infective hepatitis virus, but without symptoms, one gave a positive reaction to the

control fluid; of the 8 others 7 gave positive reactions to inactivated virus. The test appeared therefore to be useful in determining whether persons had been exposed to infective hepatitis virus or not; in contrast the percentage of persons infected with serum hepatitis who gave a positive reaction with inactivated virus (39%) was about the same as that shown by a control series of persons not known to have been exposed either to infective or to serum hepatitis. *C. L. Oakley*

2395. **P.T.A.P.: Determination of the Essential Lf Dosage**

G. Bousfield and L. B. Holt. *British Medical Journal* [*Brit. med. J.*] **2**, 73–76, July 8, 1950. 2 figs., 10 refs.

Schick-positive children from the London area received at some time between their first and second birthdays a single intramuscular injection of 0·5 ml. of samples of P.T.A.P. (an integrated diphtheria prophylactic prepared by adsorption of purified toxoid on to pure aluminium phosphate) containing 10 mg. $AlPO_4$ per ml. and carrying amounts of toxoid, with a view to determining the minimum quantity of toxoid mixed with a constant quantity of carrier that would give a satisfactory Schick-conversion rate (S.C.R.). One injection of 0·5 Lf gave an S.C.R. of 60%, and of 5 Lf gave an S.C.R. of 93·8%. It is claimed that a single dose of 5 to 10 Lf gave the maximum obtainable S.C.R. (97%) and it is suggested that the remaining 3% of children are relatively refractory to immunization with a single dose of prophylactic, however strong. Two well-spaced injections of 15 to 25 Lf of P.T.A.P. with 5 mg. of carrier give an S.C.R. of virtually 100% 2 to 3 months after the second injection.

[One hesitates to differ from a professional statistician, but it may be worth while to point out that an all-or-nothing test like the Schick test may be measuring very different things in different children, and that the heterogeneity of the responses may be much greater than the data would suggest, even when the considerable confounding is allowed for. Antitoxin determinations are essential to show up the real differences in response.]

C. L. Oakley

2396. **Quantitative Studies in Diphtheria Prophylaxis; the Second Response**

L. B. Holt. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **31**, 233–241, April, 1950. 4 figs., 7 refs.

The response of guinea-pigs to a first dose of diphtheria toxoid consists in the appearance in the blood of antitoxin after a latent period of about 3 weeks; the titre rises to a maximum level for 12 weeks. The response to a spaced second dose takes place after 3 or 4 days, and the maximum titre of antitoxin is reached in 8 to 12 days.

Toxoids adsorbed to alum (A.P.T.) or aluminium phosphate gel (P.T.A.P.) given as a primary dose cause an antitoxin response with a marked peak; this represents a second response, due to the continued presence of the antigenic stimulus, superimposed on a pure primary response.

The components of the serum antitoxin titre following a second, spaced injection are: (1) the base-line level of circulating antitoxin before the second stimulus; (2) the pure second response; (3) the contribution towards the higher base-line level of antitoxin due to the second inoculation. This elevation of the antitoxin level due to the second stimulus is greater than if the same dose had been given as a primary stimulus. Owing to this fact it is very difficult to estimate the antitoxin content of serum due to the second response alone.

Experiments reported in this paper made it possible to assess the value of the pure second response. Groups of 20 guinea-pigs were inoculated subcutaneously with 0·5 ml. of P.T.A.P. preparations containing 1 Lf per ml. of toxoid and decreasing amounts of aluminium phosphate adsorbent, and the resulting antitoxin levels were followed up for 12 weeks. The animals inoculated with the preparation giving the best response were divided into two equal subgroups. Group A was given a second inoculation identical with the first, while group B received 0·5 ml. of the preparation which had previously given the lowest primary response. The antitoxin levels were determined during a further 2-week period. In group A the resting level of antitoxin was doubled; in group B the level remained the same as that following the primary stimulus after the second response due to the secondary stimulus had receded. In both cases the pure secondary-response effect was calculated by subtracting from the total antitoxin response following the second inoculation the initial resting level of circulating antitoxin plus the antitoxin titre attributable to the second inoculation acting as a primary stimulus. The latter figure was assumed to be equal to the value obtained at the same time-interval after the first injection.

By mathematical treatment of the values obtained it was found that the percentage loss of titre per day following the second-response peak, and before the resting level had been reached, was equal to 6%; in other words, 6% of the antitoxin present at the beginning of the day had disappeared after 24 hours. Results of others working with nitrogen isotopes have indicated that the half-life of a globulin molecule is about 14 days. Taking this fact in conjunction with his own results, the author suggests that the second-response peak is due to the release of stored or reserve antibody, the supply of which is naturally not unlimited. *K. S. Zinnemann*

2397. **Observations on the Development of Diphtheria Infection after a Single Animal Inoculation with Native Anatoxin.** (Наблюдения над развитием дифтерийной инфекции у однократно привитых нативным анатоксином животных)

S. J. Fejgina. Педиатрия [*Pediatrija*] No. 3, 13–20, May–June, 1950. 2 figs., 25 refs.

Since the general introduction of anatoxin [toxoid] as diphtheria prophylactic, particularly severe cases of diphtheria have been observed with greater frequency in children who have had a one-dose immunization. The hypothesis has been advanced that the severity of the disease in these cases is due to a superimposed allergic reaction to constituents of diphtheria bacilli.

To clarify the position experiments were carried out with male guinea-pigs and rabbits. The animals were immunized with 1 ml. of one batch of anatoxin of known

potency. They were then divided into four groups. Each group was infected with a diphtheria culture after different lengths of time had elapsed. The infections were carried out on the 5th, on the 7th, on the 10th to 12th, and on the 20th days respectively after initial immunization. The infecting dose is given as 1 MLD of gravis strain No. 155, corresponding to 50 to 75 million organisms for guinea-pigs and to 200 to 250 million organisms for rabbits [volume not stated]. The injection was made into the testis.

In the first two groups there was no difference between results in immunized and in non-immunized control animals. Of 30 guinea-pigs in the 3rd group 27 died 1 to 3 days sooner than the control animals, and 15 of the former had marked local reactions consisting of appearance of a widespread, gelatinous, fibrino-haemorrhagic exudate. In the 4th group only 4 animals died within 96 hours and showed what is described as increased reactivity. Eight animals in this group were sufficiently immune to show no sign of infection.

The author admits, however, that 3 out of 30 control animals showed an increased reactivity. [It is not stated whether the controls had been injected with nutrient broth in place of anatoxin.] The increased reactivity of the controls was thought to be due to non-specific sensitization. Similar results were obtained with rabbits.

The author concludes that : (1) One ml. of anatoxin can sensitize guinea-pigs and rabbits and the sensitization can be demonstrated 7 to 12 days after the sensitizing dose. (2) A diphtheria infection after one-dose immunization may lead to an allergic reaction, resulting in severe diphtheria. (3) In a sensitized but fully immune individual allergic reactions disappear quickly. (4) The results demonstrate the inadequacy of one-dose immunization. *K. S. Zinnemann*

2398. **Relation of Nutritional Deficiency in Man to Antibody Production**
H. H. BALCH. *Journal of Immunology* [*J. Immunol.*] **64**, 397–410, May, 1950. 22 refs.

Antibody production in response to an injection of diphtheria toxoid was studied in Schick-negative patients nutritionally depleted by chronic progressive illness and in a group of Schick-negative, well-nourished patients of comparable age. The antitoxin response to a single injection of 43 Lf (0·12 mg.) of highly purified diphtheria toxoid was measured quantitatively in each case. Antitoxin levels in the blood were determined at 3-day intervals over a period of 3 weeks or longer by means of a preliminary precipitin reaction *in vitro* followed by titration *in vivo* in rabbit skin.

The anamnestic response to the single dose of antigen followed a fairly constant pattern in both groups of patients. The conclusions reached are that: (1) antibody production in man is subject to individual variation; (2) inadequate nutrition does not appreciably affect antibody production; (3) on the basis of clinical evidence there is no direct relation between antibody-producing capacity and infection; and (4) the effect of a high-protein diet on antibody production cannot be assessed from these experiments. *E. Nassau*

2399. **Antibacterial Activity of Hydrolyzed Red Blood Cells *in vitro***
D. M. WHITNEY, L. ANIGSTEIN, and D. W. MICKS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 346–350, June, 1950. 2 figs., 7 refs.

Clots of human, bovine, dog, rabbit, and chicken blood were triturated with distilled water and freeze-dried. The desiccated material was suspended in phosphate buffer at *p*H 7·8 and digested with trypsin (final concentration 1%) for 5 hours at 37° C. The resulting digest had considerable bactericidal activity against *Staphylococcus albus, Staph. aureus, Sarcina lutea, Streptococcus viridans, Bacillus subtilis, B. anthracis, B. pumilus, B. megatherium, Salmonella oranienburg, Bacterium coli*, and *Pseudomonas aeruginosa* at dilutions of at least 1 in 100. The most susceptible organisms were *B. subtilis, B. anthracis*, and *B. megatherium*.

The activity is attributed to substances liberated by the enzymatic hydrolysis of erythrocytes, digests of serum and fibrin being inactive. Hydrolysates of human and bovine blood were the most active of those tested. The optimum *p*H lies between 7 and 8; the antibacterial substance or substances concerned are heat-resistant and water-soluble, and are non-toxic to guinea-pigs and albino mice. The present authors are in favour of regarding them as antibiotics.

C. L. Oakley

2400. **The Influence of Inoculation on the Mortality and Morbidity of Paratyphoid B.** (Der Einfluss der Schutzimpfung auf Letalität und Morbidität des Paratyphus B)
H. RAETTIG. *Zeitschrift für Immunitätsforschung* [*Z. ImmunForsch.*] **107**, 388–395, June, 1950. 7 figs., 10 refs.

Subcutaneous inoculation against paratyphoid-B infection greatly reduces the severity and lethality of the disease, but does not apparently reduce its incidence in immunized persons. This reduction in severity and mortality is still evident when patients are divided into age groups; the mortality is reduced in all age groups in immunized people. Moreover there is a striking relation between percentage mortality and time after inoculation; immediately (48 hours) after inoculation the percentage mortality is higher than in the non-inoculated (suggesting a negative phase); it then falls steadily until about a year after inoculation, after which time it again rises.

Of all persons suffering from paratyphoid-B infection, the percentage immunized against it is the same as that in the general population; the total incidence of the disease shows little change from year to year.

C. L. Oakley

2401. **The Conglutination Phenomenon. VI. An Experimental Investigation of the Factors Determining the Adsorption of Complement by an Antigen–Antiserum Mixture**
A. M. BLOMFIELD, R. R. A. COOMBS, and N. H. HOLE. *Journal of Hygiene* [*J. Hyg., Camb.*] **48**, 73–95, March, 1950. 15 figs., 13 refs.

Paediatrics

2402. **On the Use of Hyaluronidase in Hypodermoclysis in Infants.** [In English]
N. HALLMAN, E. KULONEN, and O. FORSANDER. *Acta Paediatrica* [*Acta paediatr., Stockh.*] **39**, 94–101, 1950. 1 fig., 6 refs.

This is a report on the clinical use of bacterial hyaluronidase and its efficacy in comparison with the testicular product in increasing the rate of absorption in hypodermoclysis. Details of the production of crystalline hyaluronidase from a culture of a streptococcus grown in the presence of hyaluronic acid are given. This product was used in treating 32 patients of between 1 month and 2 years of age who were convalescent after an intestinal infection, and who were given infusions of saline, glucose, or glucose-saline. It was found that the rate of absorption was increased 2 to 5 times, whether bacterial or testicular enzyme was used. In no case in which the bacterial preparation was used did any undesirable side-effects develop. It is also much cheaper to produce than the testicular enzyme.

E. H. Johnson

2403. **Disturbances after Injections into the Temporal Artery in Infants.** (Troubles consécutifs aux injections pratiquées dans l'artère temporale chez des nourrissons)
R. SACREZ, P. BEYER, and M. LAGOUTIÈRE. *Pédiatrie* [*Pédiatrie*] **39**, 441–444, 1950. 4 refs.

The veins of the scalp are commonly used for transfusions in young infants. Sometimes by mistake, and sometimes deliberately, a branch of the temporal artery is used instead and the authors record some untoward vasomotor effects that have followed this procedure. The determining factors appear to be the pressure used in the injection and the degree of general vasomotor irritability of the subject. The phenomena observed are an immediate local vasoconstriction followed by vasodilatation which may reach the stage of oedema and ecchymosis and last for several days. The area affected extends, according to the severity of the reaction, from the immediate surroundings of the injection to an area bounded by the midline of the vertex, the parieto-occipital suture, the pinna, and the upper eyelid. In the case of a cachectic infant of 13 months, mydriasis, corneal ulceration, and decreased intraocular pressure were observed. While recording these findings primarily for cautionary reasons, the authors discuss briefly the nervous mechanisms involved. *T. A. A. Hunter*

2404. **Efficacy of Synthetic Antihistamine Drugs in Treatment of Acute Nutritional Disturbances in Infants.** (Efficacia degli antiistaminici di sintesi nel trattamento di disturbi acuti della nutrizione nel bambino)
A. LEONE. *Annali Italiani di Pediatria* [*Ann. ital. Pediat.*] **3**, 210–223, June, 1950. 4 figs., 26 refs.

Because of evidence previously obtained at Cagliari University that in the various forms of gastro-enteritis there is an increased amount of histamine in the blood, the author treated two groups of babies suffering from this disease with antihistaminic drugs. The first group consisted of 13 infants with "alimentary toxicosis"; 3 died. The second group included 10 babies with dysentery-like symptoms; none died.

[There is no mention of controls or of the severity of the cases.] *P. E. Polani*

2405. **A Study of Gastric Motility in Infancy.** (Studien über die Motilität des Magens im Säuglingsalter)
W. W. KELLER. *Annales Paediatrici* [*Ann. paediatr., Basel*] **174**, 273–304, May, 1950. 20 figs., bibliography.

In order to study the rate of emptying of the infantile stomach the author used the following methods. An amount of breast milk larger than the size of a normal feed was injected by stomach tube. At 20-minute intervals the stomach was aspirated and the contents measured and reintroduced into the stomach. It was found that the emptying rate was at first very rapid, then slowed down and reached a constant level, and eventually tailed off towards zero. Similarly when the emptying rate was determined over successive 20-minute periods with progressively increasing quantities of milk it was found that over a considerable range of initial volume the rate remained constant, rising only when the volume injected was about one-half the size of the normal feed. Rapid initial emptying with the larger amounts of milk is attributed to bursting open of the pylorus, and the slow rate which obtained when very small amounts of milk were injected to insufficient stimulation of peristalsis.

These findings enabled the author to elaborate a method of measuring accurately the emptying rate of the infantile stomach. A quantity of breast milk amounting to three-quarters of a normal feed is given by stomach tube, and the remaining stomach contents are aspirated after 1 hour, measured, and replaced together with additional milk to restore the original volume. By this method it was found that there was a constant individual emptying rate for each infant. If increasing amounts of milk were given it was found that the larger the child, the more rapid the emptying and the wider the range of initial volume over which a constant emptying rate was obtained. On comparing emptying rate with body surface a linear correlation was found, the emptying rate being 214 ml. per hour for each square metre of body surface. Several factors will affect the results: hunger increases the emptying rate, so that the estimation on the first specimen after fasting should be disregarded; the emptying rate becomes constant only if the child lies on its right side. The results apply to feeding with breast milk only.

The author was able to confirm his findings by experiments on the isolated stomach of infants. It was found that with increased filling the pressure in the isolated stomach rose only slightly up to a critical point, beyond which a rapid rise occurred. Once peristalsis

was stimulated, the force and frequency of the waves remained constant and were independent of the degree of filling over a wide range. *R. Schneider*

2406. **Prolonged Intravenous Drip Infusion in the Treatment of Toxicoses in Infancy.** (Tartós, vivőeres cseppinfuzio a csecsemőkori toxicosis kezelésében)
F. PÁL and B. DOMOKOS. *Orvosi Hetilap* [*Orv. Hetil.*] **91**, 900–908, July 16, 1950. 6 figs., 19 refs.

A description of the technique of intravenous infusion in infants is given, with reference to such points as choice of vein, use of needle or cannula, clotting in the needle, and the need for care in prescribing the type of solution to be used and the rate and duration of the infusion in each individual case of such conditions as acidosis, alkalosis, and anuria. The records of 5 cases are given, in which the results of laboratory investigations of the chemistry of blood and urine carried out at leisure are related to the estimate of the infant's condition made on clinical grounds alone. Owing to the need for speedy action it is on the latter that reliance must be placed at present. There is a need for rapid methods of estimating the state of electrolyte and water balance in toxaemic infants. *Dushanka Wolstenholme*

2407. **Biological Diagnosis of Influenza in Relation to Pathology of Infectious Disease in Infancy. Results of 70 Hirst Tests.** (Le diagnostic biologique de la grippe dans la pathologie infectieuse du nourrisson. Résultats de 70 réactions de Hirst)
R. A. MARQUÉZY and P. DEBRAY. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2539–2541, July 14, 1950. 3 figs.

Examination of 70 infants admitted to the Trousseau Hospital, Paris, with acute cerebral or respiratory conditions between December, 1949, and March, 1950, revealed a positive Hirst (influenza-antihaemagglutinin) reaction in 29 cases. The group with positive reactions consisted of 5 cases of diarrhoea and vomiting associated with presence of an acute neurotoxin, 20 cases of an acute respiratory condition with generalized rales over the lung fields, and 4 cases of relatively mild upper respiratory tract infection. The peak of the epidemic occurred in December, when 20 cases were recorded. The aetiological role of influenza virus is, however, obscure, since in 41 essentially similar cases admitted during the same period there was no serological evidence of viral infection. The authors suggest that these patients were possibly infected with a virus not detectable by the usual means. *J. F. McCrea*

2408. **Atypical Influenzal Pneumonia.** (La pneumonie atypique grippale)
J. MARIE, R. A. MARQUÉZY, and P. DEBRAY. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2531–2539, July 14, 1950. 17 figs., 10 refs.

The authors describe a syndrome of "atypical influenzal pneumonia" on the basis of serological examination for cold agglutinins and influenza antihaemagglutinins. Clinical observations were made on 6 children, aged 2 to 13 years, during the winter of 1949–1950. Onset of illness was usually rapid, with high fever lasting for 3 to 10 days, cough, and in some cases severe abdominal pain. Diffuse râles were present over both lung fields and nodular opacities, often resembling those of primary tuberculosis, were seen in the radiographs. Influenza-antihaemagglutinin titres of the order of 1 in 2,000 to 1 in 10,000 were found against strains PR8 and A'. [Unfortunately only one sample was taken from each patient.] A significantly raised cold-agglutinin titre (1 in 100 to 1 in 4,000) was present in 4 cases. The Paul–Bunnell reaction was negative throughout the disease. It is concluded that certain strains of influenza virus give rise to a condition closely similar to atypical pneumonia. *J. F. McCrea*

2409. **Acute Pulmonary Interstitial and Mediastinal Emphysema (Airblock) and Pneumothorax in Infancy and Early Childhood**
H. ABRAHAMSON, G. D. ROOK, and C. H. NAU. *Journal of Pediatrics* [*J. Pediat.*] **36**, 774–783, June, 1950. 7 figs., 22 refs.

Since 1939, when Hamman (*Ann. intern. Med.*, **13**, 923) and Macklin (*Arch. intern. Med.*, **64**, 913) drew attention to the occurrence of mediastinal emphysema and pneumothorax, several studies of this condition have been published. The present paper records 5 such cases in children ranging from birth to 4½ years of age. The clinical picture is one of marked dyspnoea and cyanosis, often associated with fever, and although signs of pneumothorax may be present, in most cases no obvious abnormal physical signs are present to account for the symptoms. The diagnosis is made on *x*-ray examination. Among the precipitating factors are over-zealous inflation of the lungs during artificial respiration or anaesthesia, violent strain such as occurs with persistent vomiting, asthmatic attacks, and conditions causing recurrent bouts of coughing.

In the 5 cases reported vomiting was severe in 2, asthma was present in 2, and in 1 a large amount of amniotic fluid was inhaled. The condition is benign in the majority of cases and spontaneous recovery usually occurs. No special treatment is necessary in the mild cases, but if cyanosis is present oxygen is given and chemotherapy is advisable in severe cases to prevent respiratory infection. The authors discuss the aetiology of the condition and agree with the views put forward by Macklin. *R. M. Todd*

2410. **Secretin Tests with Bilumen Gastroduodenal Drainage in Infants and Children**
G. E. GIBBS. *Pediatrics* [*Pediatrics*] **5**, 941–946, June, 1950. 1 fig., 19 refs.

A double-lumen gastro-duodenal drainage tube, which has the advantage of minimizing the dilution of duodenal contents by gastric juice and thereby permitting more accurate investigation of pancreatic secretions, is described in some detail. (There is an accompanying illustration.) With this tube the effects of secretin injection were studied in 12 normal infants and children, 11 children with fibrocystic disease of the pancreas, 2 with coeliac disease, and one each with lipoid

pneumonia and salmonella enteritis. The secretin was given intravenously in a dose of one clinical unit per kg. body weight. In the 12 normal children there was an increase of average volume of pancreatic secretion from 2·2 to 40·3 ml. in 20 minutes, an average increase in *p*H from 7·4 to 8·4, an increase in alkali titration value from 11 to 61 milliequivalents per litre, and a decrease in trypsin concentration from an average of 79 to 62, but this was offset by the increase in volume secreted. Amylase showed a 10% decrease in concentration, but this was also offset by increased volume of flow. In the 11 cases of fibrocystic disease the average volume of pancreatic secretion decreased from 2·3 to 1·9 ml. in 20 minutes, *p*H increased from 7·1 to 7·6, alkali titration value increased from 4 to 7 mEq. per litre, and trypsin concentration decreased from 0·6 to 0·3. In lipoid pneumonia and salmonella enteritis duodenal contents gave normal values with and without secretin. The author indicates that the object of using the new tube is to secure more uniform values in control patients, thereby increasing the usefulness of the test as an aid in diagnosis.

David Morris

2411. **Nocturnal Enuresis: a Special Approach to Treatment**

J. R. DAVIDSON and E. DOUGLASS. *British Medical Journal* [*Brit. med. J.*] **1**, 1345–1347, June 10, 1950. 5 refs.

An apparatus which rings a bell when an enuretic child starts micturating in bed is described, together with the results of treatment in 20 cases.

According to Strauss's classification of enuresis into primary and secondary, the children treated were all in the secondary group in which the original causative factors were perhaps no longer operative but the enuresis was self-perpetuated by anxiety. The feeling of confidence engendered by lying on a pad which let the child know immediately he started micturating played a large part in curing the condition. Personality changes followed the cure in some cases, a fact which suggests that some maladjustments may be due to enuresis rather than causative of it. In those children who did not respond to the " conditioning bell " the authors felt that the enuresis might be an enjoyable outlet.

Wilfrid Gaisford

2412. **Encopresis in Childhood.** (Encopresis im Kindesalter)

H. ALBRECHT and H. HOFFMAN. *Nervenarzt* [*Nervenarzt*] **21**, 271–281, June 20, 1950. 2 figs., 6 refs.

Encopresis is a comparatively rare habit disorder in children and adolescents who are not suffering from mental deficiency or an organic lesion affecting sphincter control. The case histories of 27 patients between 6 and 17 years old are fully reported, and are subdivided from the aetiological point of view into three groups. In the first group were those children who reacted with encopresis to a rather sudden external event which brought on a marked change in their environmental conditions. In the second group the aetiological factor was similar but of a more protracted and insidious character. To the third group belonged cases in which the environmental influences played but a small or accidental part, the psychological make-up and character of the child being of predominant importance. However, even in this third group the patient did not represent a particular constitutional type with a specific inclination to encopresis. It was found that some of the children were emotionally unstable, introverted, hypersensitive, and inclined to anxiety. The majority of the children of the first group were of a self-effacing nature and while encopresis, like many other disorders of childhood, is the result of interplay between the inborn properties of character and the environmental situation, the environmental influence was here of much greater importance.

Although often combined with enuresis, encopresis was found to be the expression of the child's reaction to a more harmful external influence and to occur in much older children, the highest proportion of cases being in the age-groups 8 to 10 and, in a lesser degree, 12 to 14. Whereas enuresis is a nocturnal disorder, encopresis is almost exclusively diurnal. Its manifestations were not limited to faecal incontinence only; faeces were used for smearing, as play material, or wrapped in paper and hidden, while even coprophagia was found occasionally. Encopresis is seen as an expression of difficulty in establishing a harmonious contact with the environment and it seems to serve the realization of pleasure by means of regression.

F. F. Kino

2413. **Evaluation of the Effect of D-Amphetamine Sulfate in the Treatment of Obesity in Children**

H. O. MOSSBERG and A. R. FRISK. *Acta Paediatrica* [*Acta paediatr., Stockh.*] **39**, 243–250, 1950.

The authors have tested the value of D-amphetamine sulphate in the treatment of obesity in 167 children between the ages of 7 and 15 years, the greatest number being between the ages of 9 and 11 years. Half were given doses of 2·5 mg. thrice daily and the remainder an identical blank pill. The diet was not strictly controlled, but is described as being high in protein with a low fat and carbohydrate content. Monthly records were made of height and weight, and 77 were re-examined after 6 months and 57 after a year. No habit was formed, but in 6 treated and 4 control cases a short period of abdominal colic or of headache and dizziness occurred.

Results were assessed by means of Rohrer's index of overweight. The weight loss, so estimated, was statistically greater in the treated group as the result of more rapid loss in the first 3 to 4 months. Thereafter the rate of loss of weight was the same in the two groups, though accurate assessment was difficult. Hunger sensations were absent in 33 of 56 treated but in only 11 of 56 control cases. The authors conclude that there is a place for the drug in the treatment of obesity in childhood and that it is without harmful effects.

A. W. Franklin

2414. **Gargoylism (Lipochondrodystrophy). A Study of Ten Cases, with Emphasis on the Formes Frustes of the Disease**

G. A. JERVIS. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **63**, 681–712, May, 1950. 10 figs., 42 refs.

Medicine: General

2415. **Resistance to Small Doses of Insulin in Various Clinical Conditions**
N. S. OLSEN and J. A. NUETZEL. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 862–866, July, 1950. 23 refs.

The effect on the blood glucose level of the injection of 0·025 unit of insulin per kg. body weight was observed in normal controls and in patients with various diseases. The difference in response in normal subjects between those on a 250-g. carbohydrate and those on a 40-g. carbohydrate diet was found not to be significant with this dosage of insulin. Patients with essential hypertension did not show any significant degree of insulin resistance, but patients with malignant hypertension were all definitely resistant ($P<0·001$). Increased resistance to insulin was also found in patients with severe infections, liver disease, neoplasms, and "collagen diseases" (rheumatic fever, rheumatoid arthritis, scleroderma, and disseminated lupus erythematosus). The hypothesis that insulin resistance in these diverse conditions may be due to increased adrenal activity in response to stress is discussed. *D. A. K. Black*

2416. **"Myoidema" and "Myotatic Irritability".**
P. L. DESHMUKH. *Indian Medical Gazette* [*Indian med. Gaz.*] **85**, 197–199, May, 1950. 4 refs.

Myotatic irritability is defined as a quick, fibrillary linear contraction of one or more muscular fasciculi produced by tapping with the finger the relaxed pectoral muscles. Myoidema is the appearance of a nodular, tumour-like swelling on squeezing, or on tapping with a patella hammer, a muscle belly. Believing that these signs are of no clinical significance, the author selected 53 young male and female subjects and found that myoidema was present in 94·4% of males and in 17·6% of females. Myotatic irritability was present in 77·7% of males and in 5·8% of females. The males who failed to react were fat, flabby, and plethoric and took no exercise. The high percentage of negative tests in the females suggests that a hormonal factor influences the irritability of muscles. *Geoffrey McComas*

ALLERGIC DISORDERS

2417. **Pyrrolazote, a Clinical Evaluation in Allergic States**
H. D. OGDEN, V. J. DERBES, and L. CULLICK. *Annals of Allergy* [*Ann. Allergy*] **8**, 293–297, May–June, 1950.

"Pyrrolazote" is a new antihistamine drug (β-pyrrolidine-ethylphenothiazine hydrochloride) and a relative of "phenergan". Tablets of 50 mg. were taken two to three times daily by 46 patients, most of whom suffered from asthma or hay-fever or both. Every other week the treatment was changed to administration of placebo tablets and the patients had to chart the number of hours during which they suffered from mild, moderate, or severe symptoms. This amounted to 10·55 hours of severe symptoms per week per patient while on placebos in comparison with 5·08 hours when on pyrrolazote. It is pointed out that not only did the condition of a number of patients improve markedly while they were taking placebo tablets, but that a great number of symptoms, such as drowsiness and nausea, appeared at the same time. Some patients were treated with a "two-stage" tablet which contained half of its substance in enteric-coated form, and the result is regarded as satisfactory, especially as side-effects appeared to be less frequent. *H. Herxheimer*

2418. **Allergy to Cold in the Respiratory System. Characteristics and Incidence in the Allergic Patient. An Experimental Study**
E. MATHOV. *Annals of Allergy* [*Ann. Allergy*] **8**, 366–372, May–June, 1950. 15 refs.

Forty patients with different allergic syndromes, mostly of the respiratory system, were investigated. Three smears of nasal mucus were obtained before and after they had placed their hands and half of their forearms in cold water at 0° to 3° C. for 10 minutes. The smears were stained with eosin and methylene blue and the number of eosinophil cells found was related to the total of all other cells. The arithmetic difference between these figures before and after testing was called the eosinophilic index. Of the patients investigated 40% complained of symptoms due to the action of cold (wind, water, temperature), but only 17·5% showed symptoms when their hands were immersed in cold water. The latter were the only patients (with one exception) who showed an increase in eosinophil index, and administration of antihistamine drugs prevented the symptoms in 5 out of 6 cases. In 2 cases a tourniquet was applied to the arms before immersion. In the first case the tourniquet prevented the expected attack of asthma which promptly developed after its removal. In the second case, the attack of intense rhinitis was not prevented by a tourniquet. In both cases administration of 0·5 mg. of histamine phosphate was followed by headache and tachycardia, but not by asthma or rhinitis. In both the reaction to cold disappeared spontaneously after a few months. *H. Herxheimer*

2419. **Allergy to Cold as an Occupational Disease. Clinical and Experimental Study on 100 Workmen in Meat-packing Factory**
E. MATHOV. *Annals of Allergy* [*Ann. Allergy*] **8**, 373–376, May–June, 1950.

Meat-packing workers engaged in work in the freezing chambers at a temperature between −3° and −30° C. were investigated for allergy to cold. About half

of the 100 studied complained of dyspnoea, rhinitis, headaches or limb pains when entering the chambers, but only one-quarter showed objective signs. Most of these (22 out of 27) were found to have an increased number of eosinophil cells in their nasal smear on exposure. The symptoms appeared in subjects with and without an allergic history, and were improved in all cases by antihistamine therapy. *H. Herxheimer*

2420. **The Bronchi during the Acute Phase of Asthma. An Experimental, Bronchoscopic, and Histological Study.** (Les bronches au cours de la crise d'asthme ; étude expérimentale, bronchoscopique et anatomopathologique)
P. VALLERY-RADOT, B. N. HALPERN, J. M. DUBOIS DE MONTREYNAUD, and V. PÉAN. *Presse Médicale* [*Pr. méd.*] **38**, 661–664, June 14, 1950. 15 figs., 13 refs.

Young guinea-pigs were sensitized with crystalline egg albumen. After 3 weeks they were exposed to aerosol inhalations of 10% ovalbumin. Examination of the killed animals revealed considerable oedema of the bronchi. It was assumed that oedema played a greater part than bronchial constriction in lethal anaphylactic shock in guinea-pigs.

In normal guinea-pigs asthma-like dyspnoea was produced by inhalation of histamine. Necropsy revealed the result of the histamine action on muscle fibres. The bronchial lumen was narrowed. Moderate capillary dilatation was seen, but no oedema. It was concluded that spasm of the bronchial muscles was the main cause of death of these animals.

The presence of bronchial oedema thus distinguishes experimental anaphylactic asthma from pharmacodynamic bronchial attacks. Antihistamine drugs, when given before the lethal inhalations, protected the animals against both types of asthma. On the other hand, the same drugs given during the attack were without effect in the anaphylactic type, whereas they acted quickly and effectively in attacks produced by histamine. The authors conclude that antihistaminic drugs can prevent the development of acute oedema, but cannot abolish oedema once it has developed. On the other hand they can completely overcome fully established bronchospasm.

Bronchoscopic examinations were carried out on human subjects before, during, and after an asthma attack. Biopsy specimens of the bronchial mucous membrane were taken during the crisis, 6 cases of "allergic" and "non-allergic" asthma being investigated. (By the term "allergic asthma" the authors mean asthma in subjects with positive skin reactions to antigens. "Non-allergic" attacks were diagnosed in patients with negative skin reactions and no history of allergic reactions.)

In allergic asthma the dominant feature was oedema, with consequent diminution of the bronchial lumen. Hypersecretion was scarce. The epithelium showed metaplasia; no eosinophil cells were seen. In non-allergic asthma, no oedema was noted. There was considerable reduction of the bronchial lumen and abundant hypersecretion. The ciliated epithelium was present. Many mucus cells were seen, and the basal membrane was enlarged. No eosinophil cells were noted. The absence of eosinophils in both types of asthma was surprising, for they were present in the blood and bronchial secretions in these cases.

Antihistaminic drugs gave favourable results in the allergic type of asthma if administered at the onset of the attack. However, the authors admit in a footnote that the response in pollen and dust asthma is less than in other allergic types. [In the abstracter's experience those two groups constitute the majority of cases of allergic asthma.] On the other hand, the non-allergic asthmatics did not respond to antihistaminic drugs. [No explanation is given for the failure of antihistaminic drugs to relieve the bronchial spasm in man.]

The experiments on guinea-pigs, as well as the bronchoscopic and histological examinations in man, show that the asthmatic allergic crisis may be attributed to acute oedema of the bronchial mucous membrane, whereas the non-allergic asthmatic attack may be due to a different mechanism. *Kate Maunsell*

2421. **Aerosols III. An Inspiration-time Meter for Quantitative Measurement of the Inhalation Period of Mists**
H. A. ABRAMSON, H. H. GETTNER, and B. SKLAROFSKY. *Annals of Allergy* [*Ann. Allergy*] **8**, 307–317, May–June, 1950. 4 figs., 5 refs.

2422. **The Use of a Combination of Two Antihistaminic Drugs in the Treatment of Allergic Vasomotor Rhinitis**
T. F. HUBBARD and A. J. BERGER. *Annals of Allergy* [*Ann. Allergy*] **8**, 350–353, May–June, 1950. 4 refs.

2423. **Idioblaptic Tobacco Sensitivity**
G. F. KNIGHT. *Annals of Allergy* [*Ann. Allergy*] **8**, 388–395, and 431, May–June, 1950. 4 figs., 9 refs.

METABOLIC DISORDERS

2424. **Cardiac Manifestations in Haemochromatosis.** (Les manifestations cardiaques des cirrhoses pigmentaires)
P. HARVIER, J. DI MATTÉO, R. DEUIL, and J. BESCOL-LIVERSAC. *Annales de Médecine* [*Ann. Méd.*] **51**, 101–151, 1950. 14 figs., 24 refs.

Among 65 cases of haemochromatosis observed since 1941 the authors have found cardiac manifestations which they considered to be attributable to the disease in 49. Cardiac failure occurred in 9 cases and was the cause of death in 8 of them, this being the most frequent cause of death in the 33 fatal cases of the series, hepatic failure and pulmonary tuberculosis (6 cases each) being the next most frequent. Failure was heralded by increasing dyspnoea followed rapidly by massive oedema and multiple serous effusions. Precordial pain, cardiac asthma, and disorders of rhythm (other than extrasystoles) were not prominent features of this type of failure, which was resistant to treatment with cardiac tonics, while mercurial diuretics proved dangerous. The remaining 40 patients showed electrocardiographic abnormalities with or without such features as hypotension, effort intolerance, and oedema. The most

constant electrocardiographic change was a distortion of the T-wave.

On histological evidence obtained from 12 necropsies the authors attribute these cardiac manifestations to a specific myocardial lesion consisting of a degeneration of the muscle fibres, followed by a replacement fibrosis and associated with, though not dependent on or proportional to, a deposition of pigment. They argue that this is but one manifestation of a widespread defect of intracellular metabolism which is the essential lesion of haemochromatosis. As such, the cardiac lesions are due to the impact of the disease itself on the cardiac muscle and are not secondary to its effects on other organs such as the endocrine glands. The paper is well illustrated with electrocardiograms and excellently reproduced photomicrographs. *T. A. A. Hunter*

2425. **Progressive Lipodystrophy. Report of Two Cases**
R. P. WARIN and J. T. INGRAM. *Lancet* [*Lancet*] **2**, 55–57, July 8, 1950. 3 figs., 17 refs.

After a fairly extensive review of the previous literature on lipodystrophy, 2 cases are recorded in detail.

The first was in a married woman of 47, in whom lipodystrophy and epilepsy both developed at the age of 26, after the birth of her first child. There was loss of subcutaneous fat down to the buttocks, the fat distribution below this being normal. This patient was subsequently admitted to a mental hospital.

The second case was in a boy aged 11, in whom the condition appeared after tooth extraction at the age of 6. The lipodystrophy affected the face and upper thorax only. This boy was abnormal mentally. The association of changes in the central nervous system with progressive lipodystrophy is discussed. *F. B. Cockett*

2426. **Clinical and Experimental Studies on Malnutrition, with Special Reference to Capillary Resistance** (Klinisch-experimentelle Untersuchungen bei Dystrophie mit besonderer Berücksichtigung der capillaren Resistenz)
W. WENDENBURG and E. ZILLMER. *Zeitschrift für Klinische Medizin* [*Z. klin. Med.*] **146**, 561–568, 1950. 1 fig., 13 refs.

A study was made between 1946 and 1949 of 180 German civilians and 220 returned prisoners-of-war suffering from malnutrition. In the civilian group hunger oedema occurred in about 15%; among the returned prisoners in 40%. In its mildest form it was present at the ankles, and with increasing severity ascended to legs, thighs, abdomen, back, and face. In some very severe cases there were ascites and pleural effusions. Among the ex-prisoners oedema frequently increased in severity for some weeks after they were put on a varied, high-calorie, high-protein diet. This is ascribed to the intake of fluids and food being much greater than the patients had been used to for a long time. Small degrees of oedema were still noticeable $1\frac{1}{2}$ years after discharge from hospital in some cases.

The fall in the level of plasma proteins was found to reflect the degree of cachexia and the severity and duration of malnutrition, but had no relation to the occurrence and extent of oedema. This showed that hunger oedema was not due solely to a fall in the osmotic pressure of the blood, the main cause being direct damage to the capillary endothelium. A simple method of estimating capillary resistance by means of a suction apparatus is described. The number of petechiae produced by the suction was roughly proportional to the degree of oedema. The capillary damage is thought to be due to the lack of several different nutritional factors and, like other effects of malnutrition, takes much longer to repair than the plasma protein level, which may be restored to normal after a few weeks of adequate diet.

Marianna Clark

2427. **Vitamin-B_6 Avitaminosis and the Curative Action of Tobacco in Pellagra.** (Vitamin B_6-Avitaminosen und Heilwirkung des Tabakgenusses bei Pellagra)
W. STEPP. *Münchener Medizinische Wochenschrift* [*Münch. med. Wschr.*] **92**, 462, June 23, 1950.

In the U.S.S.R., German prisoners of war suffering from alimentary dystrophy were given increased tobacco rations up to 20 g. a day. The Russians explained that this was suitable compensation for the lack of vitamin B_6 in the diet. The question arises whether an insufficient intake, or disturbances in the absorption, of nicotinic-amido-acids can in fact be offset by smoking.

The answer is but partly positive. Manifestations of vitamin-B_6 deficiency and pellagra are frequently found together. Both vitamin B_6 (2-methyl-3-oxy-4 : 5-bis-(oxymethyl)pyridine and nicotinic acid (pyridine-3-carboxylic acid) are derivatives of pyridinic acid, and their chemical relationship to nicotine (1-α-pyridyl-β-methylpyrrolidine) is obvious. Though the formation of vitamin B_6 from nicotine has never been proved *in vivo*, it is an established fact that nicotine is split in the human body into nicotinic acid and excreted as trigonellin (N-methylnicotinic acid). Therefore it is within the bounds of possibility that combined manifestations of vitamin-B_6 deficiency and of pellagra may be alleviated by an increased nicotine intake. *M. Dynski-Klein*

2428. **Manifestations of Pellagra and Ariboflavinosis, Particularly in Malnutrition.** (Pellagra- und Ariboflavinose-Erscheinungen besonders bei der Dystrophie)
H. BARTELHEIMER. *Zeitschrift für Klinische Medizin* [*Z. klin. Med.*] **146**, 480–508, 1950. 8 figs., bibliography.

Observations made by the author in Kiel between 1945 and 1949 on evidence of pellagra and ariboflavinosis in patients suffering from malnutrition are discussed in the light of similar reports by other authors. Of 148 patients, 54 showed pellagroid symptoms, with or without other symptoms of vitamin-B deficiency. Of these 54, 19 had intestinal and 11 neurological symptoms, the latter being commoner in conjunction with oedema. The author stresses the frequency with which minor pellagroid conditions are overlooked, especially in dermatological clinics, and cites some examples of chronic skin disorders due to this deficiency. He emphasizes the link which exists between protein deficiency and the occurrence of pellagra. A diagnosis of ariboflavinosis is less easily made, the symptoms being overlapped by those of

pellagra, and it is not so clearly linked with protein insufficiency. The author considers it to be more common than is usually accepted, expecially in diabetics. The clinical picture is often closely allied to that of sprue.

The main conclusion is that aetiologically there is the closest relationship between intestinal-tract function, protein intake, absorption, and metabolism, and B-group vitamin deficiencies. *Dushanka Wolstenholme*

2429. **Correlation of Urinary Excretion of Riboflavin with Dietary Intake and Symptoms of Ariboflavinosis**
M. K. HORWITT, C. C. HARVEY, O. W. HILLS, and E. LIEBERT. *Journal of Nutrition* [*J. Nutrit.*] **41**, 247–264, June, 1950. 11 refs.

This paper gives a summary of the findings in observations made over a period of 6 years on 66 male patients given diets containing varying amounts of riboflavin. The riboflavin was given at 8 levels of dosage, the least being 0·55 mg. daily and the highest 3·55 mg. daily. The excretion of the vitamin was measured both in 24-hour samples of urine and in samples collected during the 4 hours after the subcutaneous administration of 1 mg. riboflavin. The two series of measurements gave parallel results and showed increasing excretion with increasing intake.

Subjects consuming 0·55 mg. of riboflavin daily gradually developed signs of deficiency after 4 to 8 months. The urinary excretion also gradually fell and it seemed that a daily excretion of less than 0·1 mg. indicates a recent intake below requirements and that a daily excretion of less than 0·05 mg. indicates a prolonged dietary deficiency of the vitamin. With an intake of 1·6 mg. daily, four times as much was excreted as with an intake of 1·1 mg., which suggests that in the conditions of these experiments—in male subjects consuming 2,200 Calories daily—the requirement of riboflavin is between 1·1 mg. and 1·6 mg. daily. A depleted subject needs a daily supplement of 6 mg. for about 15 days in order to become saturated.
J. Yudkin

2430. **The Role of Glutamine in Metabolism, with Special Regard to the Formation of Uric Acid in Gout.** [In English]
A. ÖRSTRÖM and M. ÖRSTRÖM. *Acta Medica Scandinavica* [*Acta med. scand.*] **138**, 108–120, 1950. 2 figs., 28 refs.

Evidence is produced to suggest that in birds, uric acid can be synthesized from ammonia salts via glutamine and hypoxanthine. In human subjects uric acid may be derived from the breakdown of substances containing nucleic acid, either in the food (exogenous) or the tissue cells (endogenous). These two sources, however, cannot account satisfactorily for the hyperuricaemia of gout. It is therefore argued that uric acid formation in gout might take place by a process similar to that described for birds. In order to prove this, the glutamine and hypoxanthine levels were estimated in the blood of various groups of patients at the Nobel Medical Institute, Stockholm. The mean glutamine level in 15 normal subjects was found to be 9·95 mg. per 100 ml. In 8 gouty patients the mean glutamine level was much lower (1·4 mg. per 100 ml.), but the hypoxanthine level was increased. In leukaemia, glutamine and hypoxanthine levels were normal. Calculations showed that the fall in glutamine level in gout could be accounted for quantitatively by the increased formation of hypoxanthine. This suggests that the glutamine had been used up in forming hypoxanthine, which would then be available to form uric acid. *G. Ansell*

DIABETES MELLITUS

2431. **Studies on Diabetes Mellitus: The Relation of Stressful Life Situations to the Concentration of Ketone Bodies in the Blood of Diabetic and Non-diabetic Humans**
L. E. HINKLE, G. B. CONGER, and S. WOLF. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 754–769, June, 1950. 12 figs., bibliography.

The authors studied, in diabetic patients and normal persons, the effect of psychological stress (unpleasant and irritating memories) on the level of ketone bodies in the blood. At the same time glycaemic changes were observed. Levels were measured in the morning with the subjects fasting, and after a period of rest the subjects were treated to an hour of "stressful" mental reminiscences with subsequent blood analysis; these last were repeated after another, "stressless", hour. The published figures show a temporary slight rise in ketonaemia in normal persons and a more exaggerated one in diabetic patients. [Not enough detail of diet and protamine-insulin dosage is given to permit a critical appreciation of the ketonaemic state to be expected in the diabetic patients.]

The authors' figures give adequate proof of their thesis, and they suggest that the brief increase in ketosis caused by stress is due to a stimulation of the pituitary-adrenal mechanism [Selye's theory again].

[A minor point of criticism is that the authors support their arguments by reference to four unpublished papers.]
R. D. Lawrence

2432. **On the Hypoglycaemic Action of α-Tocopherol in Relation to the Route of Administration (Oral or Parenteral).** (Sull'azione ipoglicemizzante dell'α-tocoferolo in rapporto alla via di somministrazione (orale-parenterale-endovenosa)
A. BARONCHELLI. *Giornale di Clinica Medica* [*G. Clin. med.*] **31**, 410–420, April, 1950. 6 figs., 30 refs.

Because of conflicting data about the effect of vitamin E on carbohydrate metabolism the problem was reinvestigated in normal people and in rabbits. Blood sugar level was estimated by the Hagedorn–Jensen method. A 100-mg. dose of α-tocopherol caused a significant fall in fasting blood-sugar level in both man and rabbit; this fall was most profound in man when the drug was administered intramuscularly, and least when it was given by the intravenous route. In the rabbit, peroral administration was found superior to administration by other routes. In sugar tolerance tests the blood sugar curve had a lower peak and returned

earlier to the base line or even below this in men and animals given 60 mg. α-tocopherol by mouth daily for the previous 8 days. The vitamin had an identical effect on the blood sugar curve after 0·5 mg. adrenaline. In the author's opinion α-tocopherol acts on enzyme systems in liver and muscle. *Jan Brod*

2433. **Cardiovascular and Renal Findings in Long-standing Diabetes Mellitus. A Study of 221 Patients Surviving at least 15 Years.** [In English]
J. MARTENSSON. *Acta Medica Scandinavica* [*Acta med. scand.*] **138**, 94–107, 1950. 2 figs., 26 refs.

The purpose of the investigation was to determine the incidence and degree of severity of cardiovascular and renal diseases in a Swedish series of long-standing diabetics. The series comprised 221 cases (111 men, 110 women) of diabetes of 15 to 34 years' duration in patients ranging from 16 to 84 years of age at re-examination. Hypertension was present in 124 cases or 57% of the entire series, in 48% of the men, and in 65% of the women. Definite signs of arteriosclerosis of the coronary vessels were seen in 82 patients (43%) 11 of whom also had myocardial infarction. Only 6 were under 50 years of age. Gangrene, chronic ulceration, or severe arterial insufficiency of the lower extremities, was present in 42 cases (19%). In 14 cases amputation was necessary. Nephropathy was found in 71 cases (34%) with a preponderance in the younger age groups. Of the 30 cases examined post mortem 7 presented a more or less typical picture of intercapillary glomerulosclerosis. A survey is given of the incidence of co-existent cardiovascular and renal complications in the various cases.—[Author's summary.]

2434. **Degenerative Changes in Young Diabetic Patients in Relationship to Level of Control**
R. L. JACKSON, R. C. HARDIN, G. L. WALKER, A. B. HENDRICKS, and H. G. KELLY. *Pediatrics* [*Pediatrics*] **5**, 959–971, June, 1950. 24 refs,

To assess the incidence and severity of degenerative changes in diabetes and their relation to the level of control and the duration of the disease, 75 juvenile subjects with severe diabetes of over 10 years' duration were studied in great detail. Each patient was subjected to a complete physical examination, chest radiography, electrocardiography including vector leads, radiography of the pelvis and limbs for evidence of calcification of peripheral vessels, a complete eye examination, a growth study, and various biochemical investigations.

In 46·6% there were retinal changes indicating various phases of diabetic retinopathy, and there was a highly significant statistical correlation between the incidence of these and the duration of the disease, as well as the degree of deficiency of control; 14·6% had cataractous changes, but no correlation like that in retinopathy could be found. In 16·0% peripheral vessels were calcified, and again there was a highly significant statistical correlation with duration and degree of control. Neither age of onset nor severity of the disease could be related statistically to presence of retinopathy, vessel calcification, or cataract. Although 4·0% had hypertension and 4·0% had albuminuria, there were no abnormal electrocardiographic findings. In cases in which control of diabetes was poor, gains in height and weight were less than expected. The incidence of acidosis and ketosis was correlated with the incidence of lens changes. There was no correlation between plasma protein levels and any of the specified variants. The serum lipid level was consistently higher in those with poor control of diabetes and, conversely, normal levels were only found in those in whom control was excellent. The authors conclude by stressing the need for a high level of control of diabetes, because such control may delay and possibly prevent serious degenerative changes. *David Morris*

2435. **The Mental and Emotional Development of the Diabetic Child.** (Le développement mental et affectif de l'enfant diabétique)
R. BOULIN, P. UHRY, P. DUCAS, J. LAMBERT, and E. ELIACHAR. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2023–2034, June 6, 1950. 3 figs., 17 refs.

The intellectual and emotional disorders of diabetic children have not been sufficiently investigated and contradictory observations have been reported. This study is based on the examination of 30 unselected diabetic children, between 4 and 19 years old, attending out-patient clinics. Both standard intelligence tests (Binet–Simon) and projective tests (Rorschach and others) were used. The study of drawings executed by the children and the special aptitude tests were found most useful in analysing signs of emotional maladjustment.

Intelligence scores revealed that 19 out of the 30 children were below normal intelligence. The distribution was as follows: the intelligence quotient was between 60 and 69 in 4 cases, between 70 and 79 in 4, and between 80 and 89 in 11. Mental backwardness was most pronounced in children with marked physical retardation. In discussing the causes of mental deficiency in diabetic children the authors point to the multiplicity of pathological factors which may contribute, and which often vary from case to case. Neurological lesions associated with metabolic changes in the nerve cells are not infrequently associated with subclinical epilepsy. Hypothyroidism and multiglandular disturbances were seen in very few of the children. In some cases hereditary factors were the most prominent aetiological feature, in others environmental causes were more important. Educational backwardness, irregular school attendance, and an over-protective parental attitude were often found. Intellectual defects were often associated with emotional disorders, but in some cases the nervous diabetic child was found to be of very high intelligence.

The affective syndromes most frequently seen are classified as follows: emotional instability and immaturity, over-anxiety, stubbornness and aggression, and schizoid-egocentricity. The authors discuss the psychopathology of these syndromes and illustrate them with descriptions of clinical cases and test results. They believe that diabetic children are in need of special psychiatric guidance, but that they should be encouraged to lead as normal a life as possible. *J. T. Leyberg*

Cardiovascular Disorders

2436. **Acute Nonspecific Benign Pericarditis**
E. EVANS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 954–957, July 15, 1950. 3 figs., 27 refs.

The author records 11 cases of acute non-specific pericarditis of obscure aetiology. Pain was the outstanding symptom in all cases and sometimes simulated that of coronary thrombosis. The pain may be differentiated because, although it may radiate widely, even to the arms, it is aggravated by movement, respiration, and sometimes by swallowing. Fever, of variable degree, was present in all the cases. Five patients had a history of recent respiratory infection. Radiologically, 4 showed cardiac enlargement (? pericardial effusion). Electrocardiographic changes were those characteristic of pericarditis. Five of the patients had more than one attack.

The author expresses the view that this condition has no relation to constrictive pericarditis, but points out that time alone will show whether this opinion is correct. He reviews some of the literature of constrictive pericarditis and points out that its aetiology is usually obscure. In an addendum, 4 further cases are described.
M. H. Pappworth

See also Section Pathology, Abstract 2333.

2437. **Arteriosclerotic Aortic Insufficiency**
N. M. FENICHEL. *American Heart Journal* [*Amer. Heart J.*] **40**, 117–124, July, 1950. 2 figs., 8 refs.

Aortic insufficiency was noted in 17 patients, whose ages ranged from 59 to 75 and who had been known to have hypertension for from 4 to 25 years. In the only case examined post mortem (in a man aged 71) the aortic valves were fibrosed and calcified and the aorta was markedly sclerotic. In 13 of the cases the aortic insufficiency developed while the patient was under observation, but its advent appeared to have little influence on the prognosis. *C. Bruce Perry*

2438. **A Systolic Murmur Heard over the Lower Abdominal Aorta: its Significance in Peripheral Vascular Diseases**
R. J. POPKIN. *Angiology* [*Angiology*] **1**, 244–246, June, 1950. 5 refs.

The author points out that a systolic bruit over the abdominal aorta has often been noted by previous authors, but he maintains that there is no reference in either the British or the American literature to its clinical significance.

The bruit is best heard with the patient lying on his back, and the best site to listen is a few centimetres below and to the left of the umbilicus. The systolic bruit is variable in degree and duration, is not affected by posture, and is rarely accompanied by a thrill.

Out of a consecutive series of 35 patients with subjective and objective signs of peripheral vascular disease (20 had arteriosclerosis), a bruit was heard in 22 cases. In a control series of 35 patients without organic peripheral vascular disease, no murmur was heard over the abdominal aorta. The author maintains that, aneurysms and coarctation of the aorta excluded, such a bruit is pathognomonic of organic peripheral vascular disease. The abdominal aorta is the most frequent site of atherosclerosis and this change is found in some degree in the majority of people above 40. Radiological evidence of calcifications of the abdominal aorta was present in " practically all cases " of arteriosclerosis in which the bruit was heard [no figures are given]. The author discusses the possible mechanical factors responsible for the bruit. *M. H. Pappworth*

2439. **Pulmonary Embolism without Infarction.** (Embolies pulmonaires sans infarctus)
J. LENÈGRE and J. NÉEL. *Archives des Maladies du Cœur et des Vaisseaux* [*Arch. Mal. Cœur*] **43**, 385–409, 1950. 8 figs., 47 refs.

In 173 out of 500 necropsies in cases of cardiac disease pulmonary emboli or infarcts were found. In 92 of these there were one or more emboli without infarction. Such emboli may produce the symptoms of embolism without physical or radiological signs. The authors consider that the consequences and prognosis in cases of emboli which do not cause infarction are the same as in those that do. They may cause death. *D. Verel*

CARDIOGRAPHY

2440. **Studies in Intracardiac Electrography in Man. IV. The Potential Variations in the Coronary Venous System**
H. D. LEVINE and W. T. GOODALE. *Circulation* [*Circulation*] **2**, 48–59, July, 1950. 8 figs., 26 refs.

This paper from the Peter Bent Brigham Hospital and Harvard Medical School, Boston, Massachusetts, gives an analysis of the potentials recorded from a stainless-steel wire electrode passed along a catheter inserted into the coronary sinus and great and middle cardiac veins in 6 subjects with a normal heart, the tip of the electrode being passed to within 4 cm. of the tip of the catheter. Such catheterization is said to be a " relatively safe procedure ". Supraventricular premature beats occurred during manipulation of the catheter within the great cardiac vein and the coronary sinus, and ventricular premature beats with the catheter in the middle cardiac vein. With the catheter in the distal portion of the middle cardiac vein the electrocardiogram showed a ventricular R wave in one subject, and a qR wave in another, while in the proximal portion of the

vein a ventricular QS complex was recorded in one subject and an rS deflection in another. These potentials correspond respectively to left and right ventricular epicardial potentials. With the catheter in the coronary sinus and the great cardiac vein the tracings showed a large, rapid, upright auricular deflection. The ventricular complex consisted of a broad prominent Q wave followed by a prominent R wave and an inverted or biphasic T wave. It is suggested that these tracings "probably represent the composite effect of the accessible left atrial and ventricular cavity and epicardial potentials".

[This article should be read in full for its detailed description of the method of catheterization.]

William A. R. Thomson

2441. **Experimental Variations in the T-Wave of the Electrocardiogram.** [In English]
T. SJÖSTRAND. *Acta Medica Scandinavica* [*Acta med. scand.*] **138**, 191–200, July 20, 1950. 8 figs., 7 refs.

An analysis was carried out on 70 healthy subjects of the amplitude of the T-wave of the electrocardiogram in different leads under the influence of amyl nitrite, "skopyl" [methyl scopolamine nitrate], physical work, and changes of position. It was found that the T-wave diminishes linearly in amplitude with the rise in pulse frequency and generally follows the same line of regression under the influence of skopyl, physical work, moderate amyl-nitrite effect, and sometimes with changes of position. When the amyl nitrite effect was more pronounced, and frequently when there was a change in position (i.e., with the feet lower), the height of the T-wave decreased relatively more in proportion to the pulse frequency than in the other conditions mentioned. Immediately after physical work or with the head-end lowered on a tilting table, there is an increase in the amplitude of the T-wave despite a possible increase in the pulse frequency.

At a certain pulse frequency the T-wave becomes isoelectric and at higher values inverted. The isoelectric pulse value was determined on 52 healthy subjects. The frequency was found to vary between 115 and 220 per minute for T in the second limb lead and between 100 and 220 for T in lead RA VI.

The observations can be explained by the assumption that the amplitude of the T-wave depends on the contraction time and work and consequently on hemodynamic conditions. When judging the electrocardiogram in cases of suspected myocardial disease, consideration should therefore be given to physiological variability in connection with changes in the blood circulation and its regulation.—[Author's summary.]

2442. **The Relationship between the Heart Frequency and the S–T Level of the Electrocardiogram.** [In English]
T. SJÖSTRAND. *Acta Medica Scandinavica* [*Acta med. scand.*] **138**, 201–210, July 20, 1950. 9 figs., 2 refs.

The relationship of the S–T level of the electrocardiogram to the P–Q level under the influence of amyl nitrite, "skopyl"[methyl scopolamine nitrate], physical work, and changes of position has been studied on a group of 70 men and women with normal hearts. With rising pulse frequency the S–T level varies according to a curved line which displays an elevation at first and subsequently a more and more pronounced depression. Depressions of even 0·3 to 0·4 millivolts may appear in leads II, III, and RA VI in normal subjects.

The test subjects show a considerable variation with regard to the pulse frequency at which the S–T level falls below the P–Q level in leads II and RA VI. The individual subjects distribute themselves rather uniformly around a pulse rate average of about 105/ minute with extremes of 70/ minute and 135/ minute. The shift in the S–T level seems to be due to a slow change of potential after the T-wave which produces an alteration of the P–Q level in the positive direction as diastole is shortened. The S–T level thus appears to be depressed.

The observed variations would seem to be of interest in clarifying the origin of the pathological alterations which occur in the S–T segment and must be differentiated from the latter in the interpretation of clinical electrocardiograms.—[Author's summary.]

2443 (*a*). **QRS–T Patterns in Multiple Precordial Leads that may be Mistaken for Myocardial Infarction. III. Bundle Branch Block**
G. B. MYERS. *Circulation* [*Circulation*] **2**, 60–74, July, 1950. 4 figs., 11 refs.

In a discussion based upon the analysis of 4 cases of left bundle-branch block and 7 of right bundle-branch block in which the electrocardiographic findings were interpreted as indicating myocardial infarction, which was subsequently excluded at necropsy, the following points are stressed as the important ones which may lead to this mistake in diagnosis: (A) In the case of left bundle-branch block: (1) Broad, slurred QS deflections in V_1 to V_6 may occur as a result of an associated dilatation of the right atrium and ventricle, with consequent displacement of the transitional zone to the left; this is particularly likely to occur when a broad, slurred QS deflection in leads V_4, V_5, and V_6 is accompanied by an abnormally elevated, convex RS–T segment. (2) Progressive diminution of the initial R wave, and then replacement by a qRS complex as the electrode is moved towards the left. (3) An rS deflection in V_1 and/or V_2 and a QS deflection in leads farther to the left. (4) A triphasic qrS complex, consisting of small, narrow q and r deflections and a deep, broad S wave, in one or more precordial leads just to the right of the transitional zone. (5) QS or W-shaped complexes accompanied by coveplane inversion of the T wave in intermediate leads near the transitional zone. (B) In the case of right bundle-branch block: (1) In leads from the right praecordium and/or the transitional zone a minute R wave may be overlooked and the succeeding downstroke interpreted as a Q wave, and an erroneous diagnosis of septal infarction consequently made. (2) Elevation of the RS–T junction and/or abnormal inversion of the T wave in leads from the right praecordium. (3) Reduction of the R wave and deep inversion of the T wave in intermediate leads may be mistakenly taken as diagnostic of an anteroseptal infarction. (4) Concordant T waves. (5) Q waves in leads from the left praecordium may be of

such duration and such amplitude relative to the succeeding R wave, especially in the presence of left ventricular hypertrophy, as to suggest subendocardial antero-lateral infarction. *William A. R. Thomson*

2443 (*b*). **Other QRS–T Patterns that may be Mistaken for Myocardial Infarction. IV. Alterations in Blood Potassium; Myocardial Ischemia; Subepicardial Myocarditis; Distortion associated with Arrhythmias**
G. B. MYERS. *Circulation* [*Circulation*] **2**, 75–93, July, 1950. 10 figs., 47 refs.

The RS–T depression and T-wave inversion that may be found in electrocardiograms of patients with marked reduction in blood potassium level may suggest acute subendocardial infarction, while the widening of the terminal portion of the QRS complex and fusion with the T wave that may occur with marked hyperpotassaemia may suggest myocardial infarction complicated by bundle-branch block. In the differential diagnosis between acute myocardial infarction and an acute abdominal condition the finding of an abnormal RS–T complex and/or T-wave depression, with or without reciprocal elevation of RS–T segments and exaggeration of T waves in leads from the opposite wall, neither establishes the former nor excludes the latter diagnosis. In cases of subepicardial myocarditis and pericarditis the following electrocardiographic findings may be mistaken for those of myocardial infarction: (1) localized elevation of the RS–T junction and/or cove-plane inversion of the T wave in the presence of a normal or small R wave; (2) abnormal upward displacement of the RS–T segment and/or cove-plane inversion of the T wave in complexes with a distinct Q wave and a normal or borderline Q–R ratio; (3) localized reduction in amplitude of the R wave in a given lead below that attained in adjacent leads to the right and left. Disturbances of the QRS complex resembling those due to infarction may be found as a result of: (1) an ectopic ventricular focus; (2) aberrant intraventricular conduction of premature auricular beats; (3) fusion of an inverted P wave with the beginning of the QRS complex.
William A. R. Thomson

2444. **The Effect of Potassium on Inverted T Waves in Organic Heart Diseases**
M. SCHLACHMAN and B. ROSENBERG. *American Heart Journal* [*Amer. Heart J.*] **40**, 81–92, July, 1950. 5 figs., 39 refs.

The effect of the administration of potassium on the electrocardiogram was studied in 31 patients with hypertension or coronary thrombosis, whose ages ranged from 37 to 90 years and whose electrocardiograms "showed the pattern of a left ventricular hypertrophy or a myocardial infarct". Each patient was given orally 5 to 16 g. of a mixture of potassium chloride, potassium citrate, and potassium bicarbonate in a 25% solution. Electrocardiograms (standard limb leads and CF_5) were taken and the serum potassium level determined before, and 15, 30, 60, and 90 minutes after, the administration of the potassium mixture. The electrocardiogram in 9 cases showed significant changes in the T waves, a previously inverted or diphasic wave becoming upright or showing a marked decrease in the inversion. In addition, a "Wenckebach block" developed in one patient 30 minutes after ingestion of the mixture and persisted for 120 minutes, while A-V nodal rhythm developed in another an hour after taking the mixture. No changes were observed in the QRS complexes, R–ST segments, or the P waves. Seven patients complained of nausea, vomiting, or excessive perspiration. No correlation was noted between the T-wave changes, the amount of potassium administered, and the serum potassium level. The T waves reverted to their original configuration within 2 hours. As potassium is capable of altering the direction of organically inverted T waves, it is pointed out that it is of no help in differentiating "organic from functional T waves". It is suggested that potassium salts produce these changes by means of a change in the membrane potentials of the myocardial fibres.

[There is little new in these findings, but they provide useful confirmation of those of previous workers. It is unfortunate that the proportions of the three potassium salts in the mixture are not given, as it is impossible to tell how much potassium was given in individual cases. One is full of admiration for the courage of these workers in giving such large doses of potassium to individuals with damaged hearts. They were lucky to encounter no more serious reaction than a "Wenckebach block" or the conversion of a sino-auricular to a nodal rhythm. Even in apparently healthy hearts such doses of potassium have been known to produce cardiac asystole.]
William A. R. Thomson

2445. **Peri-infarction Block; Electrocardiographic Abnormality occasionally Resembling Bundle Branch Block and Local Ventricular Block of Other Types**
S. R. FIRST, R. H. BAYLEY, and D. R. BEDFORD. *Circulation* [*Circulation*] **2**, 31–36, July, 1950. 7 figs., 4 refs.

The essential electrocardiographic features of "peri-infarction block" are said to be: (1) evidence of infarction of the subendocardial myocardium of the ventricular wall or of transmural infarction with a circumferential region of subendocardial damage; (2) QRS complexes in the limb leads at least 0·11 second in duration; and (3) a characteristic QRS pattern in the unipolar precordial and extremity leads. A review carried out at the University of Oklahoma of the electrocardiograms of 464 patients with myocardial infarction revealed the characteristic features of peri-infarction block in 17 cases (nearly 4%), in 5 of which detailed records are given. The appearances described are said to develop as a rule several months after infarction. Objection is taken to the use of the term "arborization block" ". . . since its implication limits the nature of the blocking process by directly incriminating the Purkinje network and, at the same time, fails to emphasize its association with infarction". Attention is drawn to the fact that limb-lead electrocardiograms fail to differentiate peri-infarction block from bundle-branch block or intraventricular block of other types. Multiple unipolar leads are necessary for this differentiation.
William A. R. Thomson

2446. **Electrokymographic Studies of the Relationship between Electrical and Mechanical Asynchronism in the Cardiac Cycle**
P. SAMET, H. MEDNICK, and J. B. SCHWEDEL. *American Heart Journal* [*Amer. Heart J.*] **39**, 841–861, June, 1950. 6 figs., 34 refs.

Simultaneous electrokymograms of the ascending aorta and of the pulmonary artery were recorded in 83 patients with bundle-branch block, 2 patients with complete heart block with idioventricular rhythm, and during 21 premature beats in 14 patients, as well as in 25 normal young men. No correlation between electrical and mechanical ejection asynchronism was detected in 55 of the cases of bundle-branch block. Only one of the cases of complete heart block showed mechanical asynchronism, and in only 6 premature beats was the relation between the onset of ascending-aorta and pulmonary ejection abnormal. On the other hand, evidence of delayed ejection from both ventricles was found in the majority of cases.

[This is an interesting paper which deserves careful study. Lack of space prevents a summary of the various explanations advanced for the authors' findings; these should be studied in the original.]

William A. R. Thomson

2447. **Multiple-lead Electrocardiograms. Parts I and II**
I. G. W. HILL. *Lancet* [*Lancet*] **1**, 985–991, and 1027–1033, May 27 and June 3, 1950. 25 figs., bibliography.

HEART

2448. **Thyrotoxic Heart Disease. A Clinical Study of 150 Cases. I. Symptoms.** (La cardiopatia tirotoxica: un estudio clinico de 150 casos. I. Sintomas)
J. O. VAZQUEZ, A. DUQUE, P. PÉREZ GONZÁLEZ, and J. CALDERÓN. *Revista Española de Cardiología* [*Rev. esp. Cardiol.*] **4**, 250–267, May–June, 1950. 2 figs., 25 refs.

In this clinical study, based on 150 consecutive cases of thyrotoxic heart disease, it is admitted that in the more serious forms other aetiological factors may be producing the abnormal cardiac state. In a high proportion of cases, however, it is not necessary to postulate antecedent disease of the heart.

In the series there were 132 women. The mean age was 38·5 years. (Cardiac manifestations tend to appear after years of thyrotoxicosis.) There were 61 cases of Graves's disease, 31 of toxic adenoma, 13 of neurosis, and 46 unclassified. The unclassified group includes cases of monosymptomatic hyperthyroidism. There were no differences in symptomatology between the above groups, except such as may be explained by the difference in the age at which these forms are commonest. Thus the toxic adenoma group show a higher incidence of cardiac symptoms, due to the fact that this type of disease occurs at a later stage in life.

A table sets out in detail the signs and symptoms. Palpitations, dyspnoea, and oedema are the commonest symptoms. Haemoptysis was present in 5·3% of cases. Tachycardia and cardiac enlargement were the commonest signs; auricular fibrillation was present in 6% of cases. There is a detailed analysis of all the symptoms, from which a few examples of particular interest may be taken.

Oedema was present in 42·6% of patients: the commonest form was a slight swelling of the ankles in the evenings. Precordial pain occurred in 32·6% of cases. In some cases it constituted a definite anginal syndrome (11·3%). Most of these patients were over 40 years of age, and therefore it is likely that both the hyperthyroid state and coronary sclerosis were responsible for the symptoms. The authors stress the point that angina is more frequent in hyperthyroid states (11·3%) than in a non-selected group of cases of cardiac disease (3·7%). Eight patients gave a history of blood-stained sputum. In two, a mitral lesion was discovered. No pulmonary cause was found for this symptom in spite of thorough search. Tachycardia was present in 90% of cases. There was no exact correlation between the tachycardia and the basal metabolic rate. In 57 cases an apical thrill was detected. This high incidence may be due to the fact that in some cases the vibrations of the chest wall produced by a forceful impulse are wrongly interpreted as a thrill. The most noteworthy auscultatory signs were the sharp short heart sounds, specially the first mitral sound. In 48% of cases heart murmurs were present. There was a presystolic murmur in 20 cases, a systolic in 19 cases, and a double murmur in 7 cases. The authors do not think that it is theoretically more difficult to find a functional cause for a presystolic murmur than for a systolic murmur. It is considered that the high blood velocity at the end of diastole is responsible for presystolic bruits.

The blood pressure appeared to be little affected by the hyperthyroid state, though a slight increase in the pulse pressure was noted in 44·6%. Hypertension was noted more frequently in cases of toxic adenoma. Objective signs of cardiac failure were found in 15 cases only. These signs were: oedema, enlargement of liver, increased jugular pressure, and, very rarely, cyanosis.

J. J. Giraldi

2449. **Blood Flow Determination and Cardiodynamic Effects of a Venous Shunt in Pulmonary Hypertension**
R. A. HUGGINS, W. G. GLASS, D. W. CHAPMAN, and A. R. BRYAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 291–293, June, 1950. 5 refs.

Marked clinical improvement was achieved recently by Bland and Sweet (*J. Amer. med. Ass.*, 1949, **140**, 125) in 3 out of 5 patients with mitral stenosis by establishing a surgical anastomosis between the azygos vein and a branch of the right pulmonary vein for relief of the pulmonary venous hypertension. The purpose of the present experiments was to test the capacity of this type of shunt by increasing the pulmonary pressure and also to study the effects produced on the cardiodynamics.

In 10 dogs mitral stenosis was produced by suturing the left atrium above the auriculo-ventricular groove; an anastomosis between the pulmonary and azygos veins was then performed. There was no appreciable change

in the aortic blood pressure by subsequent occlusion of the left branch of the pulmonary artery or in the initial tension of the right ventricle except in one dog. The heart rate and the cardiac output were diminished when the pulmonary arterial flow was restricted or the left atrium constricted in all animals, but whether the shunt was open or closed during these two procedures seemed to have no effect on the cardiac output.

The capacity of the shunt in these acute experiments could be increased up to 8% of the cardiac output. A further attempt to increase the capacity of the shunt by rapid infusion of acacia intravenously, in an effort to increase the venous return and overload the right ventricle, was unsuccessful. There was no conclusive evidence that the presence of the venous shunt interfered with the filling of the left ventricle or that it added to the strain on the right ventricle by increasing venous return.

Z. A. Leitner

2450. **Studies on VEM and VDM in Blood in Relation to Renal Hemodynamics and Renal Oxygen Extraction in Chronic Congestive Heart Failure**

I. S. Edelman, B. W. Zweifach, D. J. W. Escher, J. Grossman, R. Mokotoff, R. E. Weston, L. Leiter, and E. Shorr. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 925–934, July, 1950. 1 fig., 29 refs.

Renal haemodynamics were studied in 12 patients with congestive heart failure and 14 controls. All the patients showed typical changes in the renal circulation, especially decrease in blood flow and decrease in oxygen consumption, despite an increased arterio-venous oxygen difference. The oxygen saturation in the renal vein and in the hepatic vein was greatly decreased in all patients. Compared with the controls, the patients had more renal vasoexcitor (VEM) in the renal venous blood, and more hepatic vasodepressor (VDM) in the hepatic venous blood. It is suggested that the production of these vasotropic factors is due not so much to the lowered oxygen consumption as to the lowered oxygen tension in the capillaries (deduced from the low venous oxygen tension). In two controls inhalation of a 10% oxygen and 90% nitrogen mixture caused the appearance of VEM in the renal venous blood. In these cases the renal oxygen consumption remained unaltered, but the arterial and venous, and therefore the capillary, oxygen tension fell significantly.

Samples of blood from peripheral arteries of controls showed no vasotropic activity. Of samples from 11 patients 2 were neutral, 5 showed a predominance of VEM, and 4 a predominance of VDM. *P. Mestitz*

2451. **Diurnal Variations of Renal Function in Congestive Heart Failure**

D. S. Baldwin, J. H. Sirota, and H. Villarreal. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 578–581, July, 1950. 9 refs.

By the use of standard clearance tests involving constant infusion of inulin it was found that in patients with congestive cardiac failure urine flow, sodium excretion, and glomerular filtration rate are greater during the night than during the day. This is the reverse of what is found in normal subjects. It was also found that the endogenous creatinine clearance is lower than the inulin clearance in patients with congestive heart failure and oedema. *G. M. Bull*

2452. **Treatment of Congestive Heart Failure in Ambulatory Patients with Salyrgan–Theophylline Administered Orally**

J. Abramson, E. Bresnick, and P. L. Sapienza. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 44–47, July 13, 1950. 6 refs.

A clinical trial was carried out, on 30 ambulant patients with congestive cardiac failure, of a mercurial diuretic in tablet form called "salyrgan-theophylline oral" ("STO"; each tablet containing 0·08 g. "salyrgan" (mersalyl) and 0·04 g. theophylline). All the patients had been receiving mercurial injections before treatment with STO, and all received digitalis, ammonium chloride, and a low-salt diet without fluid restriction during the trial. It was found necessary to administer the diuretic on successive rather than alternate days, treatment being started with a dose of one tablet thrice daily after meals for 3 successive days each week. Occasionally, greater diuresis was obtained by giving the three tablets together after breakfast. The optimum dosage was found to vary greatly from patient to patient, the largest individual dose given being 8 tablets, and the largest weekly dosage 5 tablets thrice daily for 6 days. STO completely replaced injections in 17 patients and was partly successful in 9 others. Toxicity was manifested in gingivitis and various gastro-intestinal symptoms, but only one patient could not tolerate repeated trials of the drug, owing to excessive diarrhoea. *T. Semple*

2453. **Abnormal Electrokymograms from the Wall of the Ventricle with and without Evidence of Myocardial Infarction**

F. G. Gillick and J. Schneider. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **219**, 500–512, May, 1950. 6 figs., 15 refs.

Electrokymograms were recorded on 17 patients who had had myocardial infarction, 18 patients with angina pectoris or coronary insufficiency, and 13 with "precordial discomfort" unassociated with apparent cardiovascular disease. Abnormal records of the left ventricle were obtained in 10 of the cases of myocardial infarction, 11 of those of angina pectoris or coronary insufficiency, and 10 of those of precordial discomfort. In a series of 300 consecutive routine electrokymograms, abnormal motion of the right ventricle was noted in 18 cases, and 13 of these patients had evidence of cardiac and/or pulmonary disease.

[As the authors themselves point out, "additional investigation is necessary before the full clinical significance of these observations can be established".]

William A. R. Thomson

See also Section Endocrine Disorders, Abstract 2511; and Section Disorders of the Locomotor and Osseous Systems, Abstract 2550.

DISTURBANCES OF RHYTHM

2454. **The Anomalous Motion of the Heart Border in Subjects with Gallop Rhythm or Third Heart Sounds**
J. P. BRADY and F. TAUBMAN. *American Heart Journal* [*Amer. Heart J.*] **39**, 834–840, June, 1950. 5 figs., 18 refs.

Slit kymograms, electrokymograms, and ballistocardiograms were recorded in 20 normal individuals with third heart sounds, 28 patients with protodiastolic gallop rhythm, and 7 with presystolic gallop. The electrokymograms were recorded with the patient in the supine position, and slit kymograms in the erect position. In every instance of protodiastolic gallop and third heart sound a double apical thrust in diastole was recorded, the inflection between them beginning with or slightly after the third sound. In patients with presystolic gallop rhythm, inflection of the apical thrust occurred in presystole at about the time when auricular pressure begins to fall. In 17 of the 20 normal subjects with third heart sounds electrokymograms showed protodiastolic inflection, and in 14 of these the inflections were more marked in electrokymograms from the apex than in those from the base. Of the 12 patients with gallop in whom satisfactory records were obtained, 8 showed inflections in the curve of diastolic fillings, whilst 14 of the 15 patients studied by slit kymography in the erect position showed inflections. In some patients with gallop rhythm the ballistocardiogram showed that violent movement of blood occurred in diastole, with a velocity sufficient to impart more motion to the body than occurs during systole. It is therefore suggested that " it is conceivable that such movement of blood in diastole could cause the mitral valves to be snapped shut temporarily by its reflux from the ventricle ". Although it is admitted that the findings in this report do not conclusively prove that protodiastolic sounds are due to a reflux wave closing the auriculoventricular valves momentarily, it is pointed out that this theory would fit exactly the phenomena recorded in three instances where a wave of medial movement in early diastole passed from apex to base. Attention is drawn to the experience that by slit kymography, even in the erect position, diastolic inflections coincident with gallop rhythm are detected more regularly than by electrokymographic tracings.

William A. R. Thomson

2455. **Quinidine Therapy of Auricular Fibrillation**
M. J. GOLDMAN. *American Heart Journal* [*Amer. Heart J.*] **40**, 93–99, July, 1950. 5 refs.

A series of 48 cases of auricular fibrillation were carefully studied while under treatment with quinidine. There were 28 cases of arteriosclerotic heart disease, 15 cases of rheumatic heart disease, and 4 cases of thyrotoxicosis. In one case the nature of the heart lesion was undiagnosed. Of these, 26 patients developed auricular flutter before the heart eventually reverted to normal rhythm. In 8 patients auricular flutter developed and could not be converted to normal rhythm, and in 14 cases normal rhythm returned without a stage of auricular flutter. It is concluded that auricular flutter is a common result of quinidine therapy of auricular fibrillation, and that the development of auricular flutter is not a contraindication to continuation of the drug. Further, it is claimed that cardiac enlargement and congestive failure do not in themselves contraindicate the use of quinidine.

C. Bruce Perry

2456. **Fourteen Cases of the Wolff–Parkinson–White Syndrome.** (Catorce casos de sindrome de Wolf, Parkinson y White)
M. VELA, E. BENOT, and A. ZAMBRANO. *Revista Española de Cardiología* [*Rev. esp. Cardiol.*] **4**, 195–223, May–June, 1950. 20 figs., bibliography.

The authors discuss the different theories advanced to explain the Wolff–Parkinson–White syndrome and accept with reluctance that of Wolferth and Wood. Fourteen cases of the syndrome are described. Of these 8 were in females and 6 were in males. One case occurred in the first decade, 2 in the third, 5 in the fourth, 3 in the fifth, 2 in the sixth, and one in the seventh decade. Six patients suffered from attacks of paroxysmal tachycardia. Heart disease was present in 50% of the cases; 3 had an anginal syndrome, one was the subject of cor pulmonale, one had a congenital cardiac lesion, and 2 had hypertension.

In all cases there was a short P–R interval, and this is considered the essential criterion for diagnosis. In 11 cases the QRS complex was atypical. In 12 cases the syndrome was permanent. Three patients have died, 2 in congestive failure and one in angina pectoris. Of the 11 at present alive 7 are in good health and 4 are seriously handicapped by cardiac disability.

J. J. Giraldi

2457. **Three Unusual Cases of Parasystole**
D. SCHERF and L. J. BOYD. *American Heart Journal* [*Amer. Heart J.*] **39**, 650–663, May, 1950. 8 figs., 12 refs.

Details are given of 3 cases of parasystole showing unusual features. In the first case the parasystolic rhythm was due to the activity of an ectopic centre above the bifurcation of the A-V bundle, and a periodic disturbance of the ectopic rhythm, due to a break in the " protective block ", took place. Combination beats, one of the important criteria in the diagnosis of parasystole, were absent and this is attributed to the ectopic centre being situated above the bifurcation of the A-V bundle. The periodic disturbance of the ectopic rhythm is attributed to a " supernormal phase " of the centre, which allowed it to be reached by the normal stimulus from the sinus. The unusual features of the other 2 cases were that they both showed " intermittent parasystole ", the first ectopic beat of each series being coupled to the preceding sinus beat. In one case there was a parallel variation of the sinus rate and the rate of the ectopic centre, while in the other there was an interesting intraventricular disturbance of conduction following interpolated beats. Reasons are given why the term " protective block " should be given up in the case of parasystole and be replaced by the term " protection of the ectopic parasystolic centre "—this " protec-

tion " being due to diminished excitability of the parasystolic centre. Periodic change of this excitability may be responsible for the appearance and disappearance of parasystole. Although parasystole usually develops in an abnormal heart, attention is drawn to a recent report supporting the hypothesis that it may occasionally occur in an " apparently healthy heart ".

[This interesting article (the senior author is one of the leading authorities on parasystole) deserves careful study by all cardiologists interested in a subject generally neglected in Great Britain.] *William A. R. Thomson*

CONGENITAL AFFECTIONS

2458. **Studies of the Pulmonary and Systemic Arterial Pressure in Cases of Patent Ductus Arteriosus with Special Reference to Effects of Surgical Closure**
B. E. Taylor, A. A. Pollack, H. B. Burchell, O. T. Clagett, and E. H. Wood. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 745–753, June, 1950. 8 figs., 26 refs.

The blood flow through the patent ductus arteriosus, estimated by means of cardiac catheterization in 6 cases, varied from 1·6 to 17·7 litres per minute, and from 23 to 80% of the left ventricular output in 12 cases in which it was estimated from data obtained at operation. The average pulmonary arterial pressure in 16 patients with a patent ductus lay at the upper limit of the normal range. In 7 cases direct measurement of the radial intra-arterial pressure showed a higher pulse pressure than in 7 normal controls, but the effect of exercise was within normal limits and no fall in diastolic pressure could be demonstrated. It is suggested that the finding of an apparent fall in diastolic pressure after exercise, which has been used as a diagnostic sign in this condition, is due to an error in the auscultation method of measuring blood pressure.

Closure of a patent ductus arteriosus in 15 patients caused an immediate rise in systolic and diastolic arterial pressures of about 10 mm. Hg and a fall in pulmonary arterial pressure of about 4 mm. Hg with no change in heart or respiratory rate. *D. Verel*

2459. **Truncus Aorticus. Clinical and Radiological Diagnosis.** (Le " truncus aorticus ". (Diagnostic clinique et radiologique))
P. Soulié, J. Nouaille, O. Schweisguth, and M. Touche. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **66**, 919–944, June 2, 1950. 27 figs., 20 refs.

The differentiation of the condition of " truncus aorticus " (atresia of the pulmonary artery with pulmonary blood supply through the bronchial arteries) from Fallot's tetralogy has become a matter of practical importance if unnecessary surgical exploration is to be prevented. The authors report 6 cases and stress the following diagnostic points: constant subclavicular murmur (not present in all cases); extreme aortic configuration of the heart shadow on radioscopy, with prominent aortic knuckle; absence of hilar shadows. On performing angiocardiography they found rapid filling of a large aorta, absence of the pulmonary artery, and delayed entry of the contrast medium into the pulmonary circulation. *G. Schoenewald*

2460. **The Congenital Factor in Stenosis of the Isthmus of the Aorta.** (El factor congénito en las estenosis del istmo de la aorta)
A. D. Barrios and A. L. Rodríguez. *Medicina Clínica* [*Med. clín.*] **14**, 333–338, May, 1950. 10 figs., 19 refs.

A series of embryological studies was undertaken to determine whether a congenital basis exists for the type of stenosis of the aortic isthmus seen in adults. At one stage of embryonic life a narrowing of the aortic arch appears in the region corresponding to that of a coarctation; this stenosis shows itself during the so-called post-branchial period of arterial development, coarctation being a progressive accentuation of the normal embryonic appearance. Since in all cases the congenital factor is present, there is no valid reason for dividing cases of aortic coarctation into congenital and acquired varieties. *N. M. Matheson*

2461. **Ebstein's Anomaly of the Tricuspid Valve. Report of Three Cases and Analysis of Clinical Syndrome**
M. A. Engle, T. P. B. Payne, C. Bruins, and H. B. Taussig. *Circulation* [*Circulation*] **1**, 1246–1260, June, 1950. 9 figs., 22 refs.

Three cases of Ebstein's anomaly of the heart are described, bringing the total in the literature to 26. The condition consists of a congenital weakening of the wall of the inflow tract of the right ventricle, to which is attached, either directly or by very short papillary muscles, the tricuspid valve. The result is that there is no valve between the right auricle and the right ventricle, but a small opening, which is closed during systole, between the inflow and outflow portions of the right ventricle. In the majority of cases described, the foramen ovale has been widely patent. Blood passes without hindrance from the right auricle to the upper chamber of the right ventricle but with difficulty into the lower chamber. Further, during ventricular systole, the upper chamber, though weak, contracts and forces blood back into the right auricle and probably through the foramen ovale into the left auricle.

Clinically, the onset of cyanosis is delayed and only occurs when the foramen ovale is patent, being due to the right-to-left shunt. Squatting is rare. There is enormous dilatation of the right auricle and inflow tract of the right ventricle, but signs of tricuspid incompetence, such as liver pulsation, are absent. There is no enlargement of the pulmonary artery, and the lung fields are unusually clear. Systolic and sometimes diastolic murmurs are heard; their presence is not easy to explain. Gallop rhythm is common. Electrocardiograms show auriculo-ventricular heart block and right bundle-branch block. Angiocardiograms reveal the massive dilatation of the right auricle and early filling of the left ventricle and aorta through the foramen ovale.

It is important to distinguish the condition from the tetrad of Fallot, which it resembles superficially, as it is not amenable to surgery. *C. W. C. Bain*

CORONARY INSUFFICIENCY AND ANGINA

2462. **Acute Coronary Insufficiency: Pathological and Physiological Aspects. An Analysis of Twenty-five Cases of Subendocardial Necrosis**
H. HORN, L. E. FIELD, S. DACK, and A. M. MASTER. *American Heart Journal* [*Amer. Heart J.*] **40**, 63–80, July, 1950. 14 figs., 26 refs.

The pathological changes were studied in 25 hearts with recent myocardial changes and in which acute coronary occlusion was excluded by a careful study of the coronary arteries. The lesions were almost entirely subendocardial and varied from scattered microscopic foci of necrosis to larger areas easily visible with the naked eye. The papillary muscles were particularly affected, and the changes were confined to the left ventricle. The earliest alterations consisted of defective staining of the muscle cells, with areas of haemorrhage and congestion. Later, there was obvious death of the cells with extensive haemorrhage and zones of reactive cellular infiltration. Still older lesions, with granulation tissue and fibrosis, were also seen. Coronary arteriosclerosis of varying grade was present in 19 cases, and in 22 the heart was hypertrophied. Other associated factors which appeared to play a part in the causation of this condition were aortic stenosis in 6 cases, syphilitic aortitis in one, and mitral stenosis in one. Possible precipitating factors noted were acute heart failure (5), tachycardia (5), haemorrhage (4), pulmonary embolism (3), dissecting aneurysm (2), shock (1), and infection (1). In 4 cases no such factor could be traced. It is claimed that these findings represent the permanent effects which may result from a transient discrepancy between the requirements of the myocardium and its available blood supply; this condition has been termed acute coronary insufficiency. *C. Bruce Perry*

2463. **Acute Coronary Insufficiency due to Acute Hemorrhage: an Analysis of One Hundred and Three Cases**
A. M. MASTER, S. DACK, H. HORN, B. I. FREEDMAN, and L. E. FIELD. *Circulation* [*Circulation*] **1**, 1302–1317, June, 1950. 5 figs., bibliography.

A series of 103 cases of haemorrhage, nearly all from the gastro-intestinal tract, are reviewed. In 59 of these it was considered that either clinical or electrocardiographic evidence of acute coronary insufficiency existed. Fifteen of the patients had angina pectoris and 11 congestive heart failure. Flattening or inversion of the T waves, with or without depression of the RS–T junction, was found in 53 cases. Out of 13 necropsies 4 revealed focal necroses of the subendocardial portion of the left ventricular wall and of the papillary muscles. Early blood transfusion is the best treatment.

It has long been known that angina pectoris with flattened or negative T waves may be associated with severe anaemia. It appears that in acute haemorrhage, unless a blood transfusion is given promptly, some patients may develop necrosis of the myocardium and that this may be a factor in causing death.
C. W. C. Bain

2464. **The Use of Anticoagulants in Acute Coronary Insufficiency or Impending Myocardial Infarction**
E. S. NICHOL. *Southern Medical Journal* [*Sth. med. J.*] **43**, 565–574, July, 1950. 4 figs., 21 refs.

The author believes that impending myocardial infarction may be recognized clinically by acute exacerbations, or acute development, of the syndrome of angina pectoris. Over a 3-year period 41 patients presumed to be showing the premonitory signs of infarction have been treated by the author with anticoagulants. The previous history and subsequent course of the condition made it highly probable that the diagnosis was correct. Some showed inversion or flattening of T waves in the electrocardiogram taken in the acute phase, normal appearances returning as the attack passed off, and S–T depression was also common. After initial administration of heparin, clotting was controlled by dicoumarol in most cases, though in some heparin was given throughout, the period of treatment ranging from 2 to 82 weeks. A fair degree of relief of anginal pain was obtained in all but 3 patients; 2 of the 41 patients developed transmural myocardial infarction after anticoagulant therapy had been started; 24 developed clinical manifestations of some endocardial necrosis; and 4 died with acute myocardial infarction 7 days to 10 months after stopping anticoagulant treatment.

The author admits the difficulty of differentiating with certainty between attacks of so-called "coronary failure" and frank myocardial infarction. He emphasizes the frequent benefit which seems to follow anticoagulant therapy and points out that it would be difficult to withhold therapy from a control series in order to prove the value of this line of treatment.
J. McMichael

2465. **Auscultatory Evidence of Cardiac Rupture**
F. R. NUZUM. *American Heart Journal* [*Amer. Heart J.*] **39**, 909–911, June, 1950. 1 ref.

Auscultation of the heart at the moment of rupture of the ventricular wall appears to have been reported previously only once (Reznikoff, *J. Amer. med. Ass.*, 1922, **78**, 1296), the significance of the "extraordinary sound" heard by two observers on that occasion not becoming apparent until the myocardial laceration was discovered at necropsy. In the case here reported, however, the diagnosis of cardiac rupture was made at the time and confirmed at necropsy.

The patient was a woman of 84, known to have had a high blood pressure for the last 8 years, who was admitted to hospital with a history and physical signs typical of anterior myocardial infarction of several hours' duration, this diagnosis being supported by electrocardiographic and haematological findings. The precordial friction rub which was present on admission disappeared within 24 hours and there was some clinical improvement, but an electrocardiogram on the third day suggested spread of the infarct to the posterior wall. On the morning of the fourth day the author, in the course of a routine examination, placed his stethoscope over the apex of the heart and heard several normal cycles. He describes what then occurred as follows: "While listening, there

suddenly occurred a loud, harsh murmur that filled the entire systolic period. The murmur began abruptly and ended abruptly. It was followed by four further murmurs of like description but of diminishing intensity. The murmur then disappeared entirely and the following four cycles of the heart were muffled and poorly defined. There was no detectable change in rhythm. The patient then had a convulsion and expired."

At necropsy, advanced coronary arteriosclerotic changes were found, with occlusion of the anterior descending branch of the left coronary artery and a laceration 20 mm. in length on the anterior surface of the left ventricle. *D. I. Crowther*

2466. **Results of Treatment of Coronary Arteriosclerosis with Choline**

L. M. Morrison and W. F. Gonzalez. *American Heart Journal* [*Amer. Heart J.*] **39**, 729–736, May, 1950. 23 refs.

An attempt was made to assess the value of choline in the treatment of established coronary arteriosclerosis by studying the effect on survival of its continued administration to 115 patients for periods of 1 to 3 years after an attack of coronary thrombosis, comparison being made with a control group of 115 patients (alternate cases), comparable in sex and age, who did not receive choline. [The age distribution is not given in detail for either group.] The average dose of choline bicarbonate given was 12 g. daily. Occasional unpleasant reactions were noted, including gastro-enteritis, vertigo, and body odour.

Among 52 patients who were treated for a period of one year, 4 deaths occurred during treatment, whereas 10 deaths occurred in the corresponding group of 52 controls during the same period. Five deaths occurred among 35 patients treated for 2 years, and 12 among the 35 controls during that time, while 5 deaths occurred among 28 patients treated for 3 years, 13 of the controls of this group having died during this time. There were 19 deaths from recurrent coronary thrombosis among the controls and 6 in treated cases. *J. W. Litchfield*

2467. **Endoscopic Sympathotomy in Angina Pectoris.** (Die endoskopische Sympathikotomie bei Angina pectoris)

E. Kux and R. Vetter. *Deutsche Medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **75**, 747–751, June 2, 1950. 5 figs., 16 refs.

In 3 cases of anginal pain the authors, after induction of a left pneumothorax, severed endoscopically the left sympathetic chain between the levels of T1 and T5 and infiltrated the stellate ganglion with procaine. Subsequent observation over a period of 12 months showed that there had been complete abolition of the anginal attacks. In the first case an abnormal electrocardiogram became normal within 5 weeks of the operation. [The history of this patient and the tracings reproduced do not exclude the occurrence of a coronary occlusion just before the operation. The second patient had a history of rheumatic fever and decubitus angina as well as angina of effort, and the blood-pressure figures suggest aortic incompetence.] *G. Schoenewald*

HYPERTENSION

2468. **The Response of the Flicker Fusion Threshold to Nitroglycerin and Its Potential Value in the Diagnosis, Prognosis, and Therapy of Subclinical and Clinical Cardiovascular Disease**

L. R. Krasno and A. C. Ivy. *Circulation* [*Circulation*] **1**, 1267–1276, June, 1950. 3 figs., 12 refs.

It has been found that the frequency with which successive flashes of light must occur to appear as a beam, free from flicker, is fairly constant in normal subjects. A 60-cycle alternating lamp is free from flicker; a 40-cycle lamp would appear to flicker to all normal people, and a 50-cycle lamp to some. The average figure at which flicker is normally observed is about 45 flashes per second. This is called the flicker-fusion threshold and an instrument, the flicker meter, has been constructed for testing it. The threshold is lowered by fatigue, smoking, or a heavy meal.

On the assumptions that: (1) gross retinal changes in hypertension are preceded by spasm of the arterioles; (2) this spasm could be abolished temporarily by giving nitroglycerin; (?) spasm of the retinal arteries might be accompanied by spasm of the coronary arterioles, a "nitroglycerin flicker test" was devised. The flicker-fusion threshold is determined, the patient chews a tablet of nitroglycerin, and the test is repeated three times at 2-minute intervals. In normal subjects, the threshold is either unaffected by nitroglycerin or it is lowered owing to passive congestion of the vessels. In 139 patients with hypertension the threshold rose considerably after nitroglycerin; in 17 with infarcts or angina a moderate rise occurred.

It is suggested that the test may prove helpful in detecting early cases of hypertension, and in the diagnosis of angina pectoris when the evidence otherwise is doubtful. *C. W. C. Bain*

2469. **Haemodynamic Studies on the Mechanism of the Effect of Sympathectomy in Hypertension.** (Hämodynamische Untersuchungen zur Frage des Wirkungsmechanismus der Sympathektomie beim Hochdruck)

O. Bayer, E. Boden, H. Boeminghaus, and S. Effert. *Zeitschrift für Klinische Medizin* [*Z. klin. Med.*] **146**, 607–632, 1950. 4 figs., 42 refs.

This is a report of 18 cases of hypertension treated by bilateral sympathectomy according to the method of Boeminghaus, which is described. Cardiac output per beat and per minute, vascular elasticity, and total peripheral resistance were estimated by the sphygmographic method of Bromser and Ranke. Estimations were made before and immediately after sympathectomy, and again between 6 and 18 months after operation. They showed that in the cases where hypertension was due to increased cardiac output without marked increase in peripheral resistance, the fall in blood pressure after operation was due to a decrease in cardiac output. Where loss of elasticity and high peripheral resistance were the causes of hypertension the fall in blood pressure was due either to a lowering of that resistance or again solely to a decrease in output. Electrocardiograms taken

before and after operation reflected the improvement in the nutrition and action of the heart muscle. Pre-operative peridural injections of procaine were made at the level of the 8th or 9th dorsal segment. The fall in blood pressure which followed this procedure was in general due to the same factors as that of the subsequent sympathectomy in any one case, but the test does not permit of a reliable forecast of the behaviour of the blood pressure after operation.

In the patients with hypertension due to increased cardiac output there were orthostatic circulatory disturbances for a short time after operation. In almost all cases the blood pressure rose again slowly after operation, though not to its high pre-operative level. The most impressive clinical finding after operation was a marked improvement in general well-being due, in particular, to an amelioration of the headache from which all patients had suffered. *Marianna Clark*

2470. **Extensive Laboratory Studies of a Patient with Pheochromocytoma before and after Successful Operation, with a Note on the Trial of Piperidylmethyl Benzodioxane to Differentiate such Conditions from Essential Hypertensive Vascular Disease**
R. W. WILKINS, W. E. R. GREER, J. W. CULBERTSON, M. H. HALPERIN, J. LITTER, C. H. BURNETT, and R. H. SMITHWICK. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 51–78, July, 1950. 13 figs., 30 refs.

A case of phaeochromocytoma of the right adrenal gland was investigated at the Massachusetts Memorial Hospital. The patient was a man, aged 22 years. Arterial hypertensive disease was diagnosed when, at the age of 20 years, he was believed to have experienced a transient attack of hypertensive vascular encephalopathy. Detailed investigations were made before operation for the removal of the phaeochromocytoma. A fluctuating increase in the arterial blood pressure was demonstrated on clinical examination. In addition, the patient suffered from hyperhidrosis and bouts of fever. Other findings included hypertensive vascular retinopathy and postural tachycardia. An increase was observed in the basal metabolic rate, in the cardiac output, and in the hepatic portal blood flow and oxygen consumption. There was a rise in the fasting level of blood sugar, and dextrose tolerance was found to be reduced. Urine tests showed that the patient was subject to intermittent attacks of albuminuria and glycosuria. A decrease in the renal blood flow was detected. The histamine and benzodioxane reactions were positive. There was also a slight decrease in sensitivity to the intravenous injection of small quantities of adrenaline. After the removal of the tumour the patient became free from symptoms and from almost every abnormality, but there was no improvement in the renal function, and the electrocardiogram indicated the presence of an infarct in the posterior wall of the heart

An attempt was made to determine whether intravenous injection of piperidylmethyl benzodioxane could be used as a test in the diagnosis of phaeochromocytoma. The test was employed in experiments on 75 patients suffering from hypertension due to various causes, but side-effects occurred in 28 cases. Moreover, the injections failed to provide uniformly reliable results. Some of the side-effects were severe, for the reactions included convulsive movements, precordial pain, and a pronounced rise in the arterial blood pressure. *A. Garland*

2471. **Diagnosis of Pheochromocytoma by the Adrenergic Blocking Action of Benzodioxane**
M. GOLDENBERG and H. ARANOW. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1139–1143, July 29, 1950. 4 figs., 14 refs.

"Benzodioxane" (2-[1-piperidylmethyl]-1 : 4-benzodioxane), administered intravenously, caused a transitory reduction of blood pressure in 11 out of 12 cases of persistent hypertension associated with phaeochromocytoma. Chemical analysis of 8 of the tumours removed at operation showed that a positive benzodioxane test occurred in tumours containing either adrenaline or noradrenaline. Administration of benzodioxane also decreased the hypertension produced in normal subjects by the intravenous infusion of noradrenaline. The higher the blood pressure, the more marked was the decrease. In cases of hypertension from other causes there was no change or a rise in blood pressure following the administration of benzodioxane.

After the removal of phaeochromocytomata in patients with persistent hypertension the blood pressure does not always fall to normal, and it is postulated that some secondary hypertensive mechanism is acting in these cases. It is also suggested that a negative benzodioxane test in a case of phaeochromocytoma with persistent hypertension may be due to the temporary absence of excess circulating adrenaline. In one case of phaeochromocytoma the fall in blood pressure produced by benzodioxane was followed by a temporary but marked rise. This was attributed to the sudden liberation of an unusually large amount of adrenaline or noradrenaline into the circulation. *G. Ansell*

2472. **The Effect of "Rice Diet" on Plasma Volume and Extracellular Fluid Space in Hypertensive Subjects**
R. J. F. MURPHY. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 912–917, July, 1950. 1 fig., 24 refs.

In a series of 17 patients, plasma volume (by the Evans blue method) and extracellular fluid volume (by the thiocyanate space method) were measured before and after a period of from 10 to 14 weeks on the Kempner rice diet. There was generally a fall in both plasma and extracellular fluid volume. This was not closely correlated with the weight loss. The serum sodium concentration was well maintained, but the total amount of extracellular sodium fell in proportion to the fall in extracellular fluid volume. Most of the patients were hypertensive, and it cannot be assumed that normal subjects would show similar changes.

D. A. K. Black

2473. **Hypertensive Ulcer of the Leg**
F. MARTORELL. *Angiology* [*Angiology*] **1**, 133–140, April, 1950. 3 figs., 10 refs.

Disorders of the Blood

2474. **Lipomelanic Reticulosis**
C. M. AGRESS and H. C. FISHMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 957–960, July 15, 1950. 1 fig., 4 refs.

The authors, from Los Angeles County General Hospital, record 4 cases of a rare type of reticulosis, the main features of which are a skin lesion and a generalized lymphadenopathy. There have been only 2 American papers and one French paper on this subject; the authors review these.

The skin lesion is variable but usually consists of a generalized, lichenified or eczematous, very chronic lesion with pigmentation and marked pruritus. The nails are often affected and there may be loss of hair from the scalp and axillae. The authors describe the histological changes in the skin, which are apparently variable and vague. The lymph nodes, however, always show the same changes, with disorganization and reticular proliferation, many eosinophils and histiocytes being present. Correct staining reveals melanin and fat in large amounts. The condition may clinically resemble lymphadenoma, especially as the blood in some of the patients shows an eosinophilia. Differentiation is important, because lipomelanic reticulosis is associated with a good prognosis. *M. H. Pappworth*

2475. **The Early Diagnosis of Sarcomata of the Lymphoid Tissues.** (Le diagnostic précoce des sarcomes des organes lymphoïdes)
B. DREYFUS and R. ANDRÉ. *Revue d'Hématologie* [*Rev. Hémat.*] **5**, 57–77, 1950. 39 refs.

2476. **Studies on a Case of Acute Antithromboplastinemia**
W. J. HARRINGTON, J. F. DESFORGES, F. STOHLMAN, C. B. CROW, and W. C. MOLONEY. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 87–92, July, 1950. 21 refs.

The case is presented of a woman in whom, without obvious reason, a haemorrhagic tendency developed for the first time at the age of 60. Investigation revealed a coagulation defect characterized by defective prothrombin conversion associated with a prothrombin time (as measured by the one-stage method) which was prolonged when human, but normal when rabbit, brain thromboplastin was employed. The specificity of this effect was confirmed by additional use of various specimens of brain thromboplastin from other animals. It was found also that any mixture which contained the patient's whole or prothrombin-free plasma prolonged the prothrombin time of normal plasma when human thromboplastin was used. There was no evidence that normal plasma supplied a factor missing from the patient's plasma, and no evidence of the presence of abnormal prothrombin or antiprothrombin in the patient's plasma. *A. Brown*

2477. **Purpura in Pregnancy. With Special Reference to Idiopathic Thrombocytopenic Purpura**
H. N. ROBSON and L. S. P. DAVIDSON. *Lancet* [*Lancet*] **2**, 164–169, July 29, 1950. 53 refs.

From a review of 95 published cases of purpura in pregnancy it is concluded that 21 can reasonably be accepted as examples of idiopathic thrombocytopenic purpura. The authors add a further 4 cases of this condition. The maternal mortality in these 25 cases, involving 34 pregnancies, was 8%. The infant mortality was 25%. Most of the recorded deaths occurred in the early months of pregnancy. Bleeding at delivery was rarely excessive. Thrombocytopenia in the infant was common but usually transient. There is no evidence that pregnancy significantly influences the course of the disease. *A. Brown*

2478. **Aminopterin in Treatment of Leukemia in Children. Serial Aspirations of Bone Marrow as a Guide to Management and Appraisal of Treatment**
C. H. SMITH and W. R. BELL. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **79**, 1031–1048, June, 1950. 4 figs., 21 refs.

If a remission in leukaemia is " an essentially complete restoration of normal haematological function and health ", then only in one of the 13 cases of acute leukaemia in children discussed in this paper was this requirement fulfilled. Remission rates in treated and untreated leukaemia are similar. The authors discuss some cases treated by them, 12 being given " aminopterin " intramuscularly in doses of 0·5 to 1·0 mg. daily (rather more in refractory cases). Total dosage ranged from 6 to 54 mg. One child was given " amethopterin " in oral dosage of 2·5 to 5 mg. daily. Adjuvant treatment with penicillin, aureomycin, transfusion of blood, hesperidin, and vitamin C was also employed.

Serial bone-marrow examinations, generally once weekly, were found to provide the most reliable index of inhibitory effect of the drug. A reduction of the total nucleated count from the normal childhood level of 100,000 to 150,000 per c.mm. to about 30,000 per c.mm. was aimed at. Reappearance of normoblasts and megakaryocytes in bone marrow, and of polymorphonuclears in marrow and peripheral blood, was looked upon as a favourable sign. These cells were chosen as indices because they can be recognized with certainty.

The most satisfactory haematological responses occurred in acute lymphoblastic leukaemia. Three cases of myelogenous leukaemia were little influenced. When the dosage is controlled by marrow counts in this way, toxic effects of drugs are few. In this series buccal ulceration was the most common, and alopecia less so.

Survival of these children appeared to be no longer than in a group untreated with folic-acid antagonists, but accuracy of comparison is difficult because of the

insidious onset of the disease. Most treated patients died within 6 months of onset of leukaemia; one lived for more than 12 months. *M. MacGregor*

2479. **Studies on the Measurement of Erythrocytes in Tropical West Africa and Description of a Macroplania in Negroes with Pneumonia.** (Erythrozytometrische Studien im tropischen Westafrika und Beschreibung einer Makroplanie beim pneumoniekranken Neger)
E. H. MAIER. *Zeitschrift für Tropenmedizin und Parasitologie* [*Z. Tropenmed. Parasit.*] **2**, 59–68, July, 1950. 23 refs.

Measurements of the erythrocytes in Africans in Fernando Po, Spanish Guinea, were made difficult because of the frequency of chronic malaria. Febrile conditions, especially pneumonia, are thought to produce large, flattened erythrocytes. *G. M. Findlay*

2480. **Studies with Inagglutinable Erythrocyte Counts. I. A Method for Measurement of Net Gain or Deficit of Red Cells in the Human Subject**
E. L. DEGOWIN, R. F. SHEETS, and H. E. HAMILTON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 693–713. June, 1950. 8 figs., 40 refs.

2481. **Studies with Inagglutinable Erythrocyte Counts. II. Analysis of Mechanism of Cooley's Anemia**
H. E. HAMILTON, R. F. SHEETS, and E. L. DEGOWIN. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 714–722, June, 1950. 3 figs., 14 refs.

ANAEMIA

2482. **Effect of Metal-combining Globulin (Fraction IV-7) in Severe Mediterranean Anemia**
T. R. C. SISSON, C. H. SMITH, R. W. BONSNES, S. SIEGAL, and S. STOCK. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 258–261, June, 1950. 6 refs.

Iron is transported in the serum only in attachment to a β_1-globulin, the " metal-combining globulin ", which resides in fraction IV-7 of the plasma. Normally this globulin is not completely saturated with iron, and its latent iron-combining capacity is measurable by the addition of known quantities of iron to different volumes of serum until a colour change indicates complete saturation. The total iron-combining capacity of the serum is the sum of the serum iron level and the latent iron-binding capacity. It has been shown (Smith *et al.*, *Pediatrics*, 1950, **5**, 799) that in children with severe Mediterranean anaemia the serum iron content is increased and there is no latent iron-combining capacity, whereas normally the serum iron level is about one-third of the total capacity. Comparable changes were seen in children with spherocytic and sickle-cell anaemias.

Fraction IV-7 of the plasma in purified form was administered intravenously in 4 cases of severe Mediterranean anaemia in doses of 4 to 10 g. in 500 ml. normal sodium chloride solution. All subjects showed a rise in serum iron value lasting for 3 to 5 hours and the transitory appearance of a latent iron-combining capacity. In one subject the latter only appeared after the administration of 20 g. of fraction IV-7. In a child with severe sickle-cell anaemia the serum iron level rose from 245 μg. per 100 ml. to 310 μg. per ml. approximately 4 hours after the administration of 5 g. of fraction IV-7, but no latent iron-combining capacity appeared. These observations suggest the release of iron from the tissues to the blood when additional metal-combining globulin is supplied. *A. W. H. Foxell*

2483. **Reticulocyte Ripening in Experimental Anemia and Hypoproteinemia. Effect of Amino Acids *in vitro***
A. NIZET and F. S. ROBSCHEIT-ROBBINS. *Blood* [*Blood*] **5**, 648–659, July, 1950. 21 refs.

A special technique is described for measuring the ripening time of reticulocytes. Heparinized blood is incubated with brilliant cresyl blue and smears examined under dark-ground illumination because this allows reticulum granules to be distinguished from other inclusions, such as Heinz bodies. The reticulocytes are then classified according to the amount and disposal of reticular substance into five groups corresponding to their degree of maturity (Nizet, *Acta biol. belg.*, 1941, **1**, 402). To compare the reticulocyte ripening time in the same blood under different conditions the range of decrease in the total number of young reticulocytes after incubation for a given time is determined in each case. In comparing the blood of different animals, the ripening time for each group, that is, the time taken for total transfer to the next group, is estimated and the ripening times of corresponding groups are compared.

These techniques were applied in studying reticulocyte ripening *in vitro* in the blood of dogs rendered anaemic by haemorrhage and given either (1) a diet low in iron but containing a basal allowance of protein; or (2) a basal non-protein diet. It was shown that in group (1) reticulocyte ripening proceeds as in non-anaemic dogs receiving the same diet, whereas in group (2) there was a block of the ripening effect. It was found that this block in reticulocyte ripening ran parallel with failure of haemoglobin regeneration, and that if a diet permitting haemoglobin regeneration is then given the reticulocyte ripening time also returns to normal. Experiments have shown that 10 amino-acids and glycine are essential for growth. If a mixture of these is added to blood showing delayed reticulocyte ripening *in vitro* the reticulum then ripens and disappears in normal time.
M. C. G. Israëls

2484. **The Long-term Evaluation of Folic Acid in the Treatment of Pernicious Anemia**
S. O. SCHWARTZ, S. R. KAPLAN, and B. E. ARMSTRONG. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **35**, 894–898, June, 1950. 2 figs., 21 refs.

A group of 98 patients with pernicious anaemia who were being maintained satisfactorily on liver treatment were given folic acid (pteroylglutamic acid), 5 mg. daily by mouth, instead of liver. After 3½ years only 12 remained well and were still having this treatment. Of the 86 others 23 developed signs of involvement of the

central nervous system, in 23 the erythrocyte count fell and bone-marrow studies showed that a true relapse was in train, 9 suffered a combined haematological and neurological relapse, and 3 had to abandon the treatment because of sore tongue or weight loss. The remaining 26 patients are made up of 14 who objected to taking pills and 12 who were lost sight of. In nearly all cases the relapses were successfully reversed by liver treatment; the exceptions were 8 patients who developed disease of the central nervous system and were not relieved even after 6 months' intensive liver treatment.

Most of the neurological relapses occurred between 1 and 2 years after the start of treatment and none later than 2 years after. The haematological relapses were spread over 3 years and almost as many occurred in the third year as in the first two together. This difference of timing suggests that neurological and haematological relapses are due to different causes. The haematological relapses in the series treated with folic acid are compared with the spontaneous relapses occurring in a group of 41 patients who had stopped liver treatment, most of which were within 12 months of ceasing treatment, a few within 2 years, and very few between 2 and 3 years. This difference gives a measure of the effectiveness of folic acid in maintaining haematological remission in pernicious anaemia. It is suggested that folic acid acts either by utilizing or by making utilizable other growth substances still available, and fails when the latter are exhausted. The authors emphasize that long-term studies are essential before it can be decided whether a substance is really effective in the treatment of pernicious anaemia. *M. C. G. Israëls*

2485. **Cold Agglutinins as the Cause of Chronic Haemolytic Anaemias.** (Kältehämagglutinine als Ursache chronischer hämolytischer Anämien)
H. SCHUBOTHE and H. W. ALTMANN. *Zeitschrift für Klinische Medizin* [*Z. klin. Med.*] **146**, 428–479, 1950. 13 figs., bibliography.

In a lengthy paper the authors review present knowledge of cold agglutination, describe their own findings in certain cases, and discuss their significance. They are particularly interested in four facts: (*a*) the finding of cold-agglutinin titres of 1 in 16 in normal people, which may be evidence of previous infection; (*b*) after such illnesses as atypical pneumonia and trypanosomiasis the cold-agglutinin titre usually decreases, but in a few cases remains persistently high; (*c*) cold agglutinins may be active at temperatures up to 30° C.; and (*d*) although the agglutination with cold agglutinins is reversible at higher temperatures, the freed erythrocytes have a much increased fragility.

Two cases are described in great detail, the report of one, which ended fatally, including post-mortem findings. Despite difficulty in tracing a history of previous infection, these appeared to be cases in which a chronic haemolytic anaemia, without crises, was brought about by the action of cold agglutinins. In the opinion of the authors such cases can be recognized clinically by the occurrence of acrocyanosis on short exposure to cold and its disappearance on regaining warmth, intermittent icterus after cold, and chronic anaemia despite protection from cold. The cold-agglutinin titre is between 1 in 100,000 and 1 in 300,000, the agglutinins are non-specific, thermostable, and active at temperatures as high as 20° or 30° C., and the agglutination is reversible at higher temperatures. Agglutination will be found post mortem in the bone marrow, liver, spleen, and muscles, with much evidence of phagocytosis of erythrocytes by the reticulo-endothelial system, especially in the liver.

Dushanka Wolstenholme

2486. **Hemolytic Anemia with Paroxysmal Methemoglobinemia and Sulfhemoglobinemia. Report of Two Cases**
A. S. EVANS, N. ENZER, H. A. EDER, and C. A. FINCH. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 22–34, July, 1950. 5 figs., 15 refs.

In the first case described, in a woman aged 37, cyanosis of varying intensity, accompanied by haemolytic anaemia, had been present since the age of 16, when it appeared suddenly during treatment of a respiratory infection with an unidentified drug. At 35 she began to have attacks of weakness, fainting, dyspnoea, tachycardia, fever, and sternal and abdominal pain, associated with increasing cyanosis. No abnormal pigments were found in urine or plasma, but intracellular methaemoglobin was present in concentration varying from 3% to 38%, with fluctuations of 20% in 12 hours, and sulphaemoglobin in concentration of 3% to 8%. The ability of the erythrocytes to reduce methaemoglobin was only slightly impaired. No abnormal oxidizing agents could be demonstrated in the serum. Ascorbic acid therapy was ineffective; taking methylene blue relieved cyanosis, but not other symptoms, for a period of 24 hours.

The second patient, a woman aged 29, had complained for 5 years of fever, rigors, and pain in the right flank, and for 3 months of blueness of the skin and passage of brown urine, later accompanied by weakness, unconsciousness, and occasional chest pain. A severe haemolytic anaemia was present and improved after splenectomy, but cyanosis and pain in the side persisted. The urine varied in colour from clear yellow to port-wine or coffee, but contained no demonstrable blood, melanin, homogentisic acid, haemosiderin, porphobilinogen, methaemoglobin, or porphyrin. The findings in the blood and the response to ascorbic acid and methylene blue resembled those in the first case, but the test for oxidizing agents in the serum was positive. The cyanosis was eventually completely relieved by removal of the right kidney, which contained multiple abscesses infected with a nitrite-producing bacillus.

The authors comment that the rapid fluctuation in methaemoglobin concentration and the ineffectiveness of ascorbic acid therapy in these cases are typical of the " enterogenous cyanosis " group associated with the presence of circulating oxidants (nitrites), in contrast to the cases of congenital defect in which methaemoglobinaemia depends on failure of the normal intracellular methaemoglobin-reducing system. The accompanying haemolysis may be due to direct action on the erythrocytes of the pigment-producing compound, or to increased destructibility of the cells following interference with their reducing-enzyme systems. *H. McC. Giles*

Respiratory Disorders

2487. **Air Velocity Index. A Numerical Expression of the Functionally Effective Portion of Ventilation**
E. A. GAENSLER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 17–28, July, 1950. 3 figs., 15 refs.

The author describes the determination of the "air velocity index" as a measure of ventilation in tests on 435 patients on 476 occasions. In the past it has been found that a direct comparison between the vital capacity and the maximum breathing capacity is misleading. By using appropriate formulae to correct for age, sex, height, and weight it is possible to predict the normal vital capacity and maximum breathing capacity for any given age, sex, height, weight, and body surface. The ratio of the value actually found, expressed as

$$\frac{\text{percentage of maximum predicted breathing capacity}}{\text{percentage of predicted vital capacity}},$$

is known as the air velocity index.

From experiments, it was found that this index was increased in patients with loss of pulmonary tissue due to disease or to collapse treatment, the increase being approximately proportional to the amount of loss of tissue. On the other hand bronchial obstruction and loss of pulmonary elasticity decreased the air velocity index. *R. H. J. Fanthorpe*

2488. **Disseminated Pulmonary Calcification. A Report of 114 Cases with Observations of an Antecedent Pulmonary Disease in 15 Individuals**
F. C. WHITE and H. E. HILL. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 1–16, July, 1950. 9 figs., 44 refs.

A series of 114 cases of disseminated pulmonary calcification encountered in the Ray Brook State Tuberculosis Hospital district, New York, is reviewed. In 15 cases clinical, as well as radiological, observation was possible. A brief review of the literature is given and the frequent association of pulmonary calcification with a positive histoplasmin skin reaction is noted.

In all patients under review a complete history was obtained and clinical and radiological examinations were made, together with tuberculin and histoplasmin skin tests.

Of the 114 patients 106 were found to have spent at least two-thirds of their lives in rural areas and 84% were engaged in farming or similar rural occupations; 12 of the 18 patients who were non-rural residents had been exposed to dust about the habitat of pigeons; 95% of patients gave a history of exposure to dust either from threshing or about the habitat of pigeons or domestic fowl. The period of observation varied from a single visit to 16 years.

In the majority of patients there were no abnormal physical signs on examination, though a typical radiological picture of multiple disseminated calcified foci existed in both lung fields. Tuberculin and histoplasmin skin tests were carried out on 84 of the 114 patients; 94% reacted to histoplasmin and 52·4% to tuberculin, while 44% reacted to histoplasmin alone, 2·4% to tuberculin alone, and 3·6% to neither antigen. Of 305 comparable patients without pulmonary calcification used as controls 14·2% reacted to histoplasmin and 29·8% to tuberculin.

In 15 of the cases reviewed, a history of a chronic pulmonary disease was obtained, and in 12 of these the natural history of the condition was studied from onset to the development of calcification in the lung. Of these 13 reacted to histoplasmin and 9 to tuberculin, and 8 patients reacted positively to the complement-fixation test for histoplasmosis. One necropsy is reported, the patient having died as the result of an accident; discrete calcified nodules were found in the lungs and were surrounded by hyalinized fibrous tissue without any giant cells.

The authors suggest that there is some relation between this disease and the inhalation of organic dust by farmers in valley regions. The fact that the condition is not a constant finding in rural communities suggests that the dust may be carrying the causal organism. They incline to the view that this organism is probably *Histoplasma capsulatum* but stress the need for further investigations to establish this theory
R. H. J. Fanthorpe

2489. **Pulmonary Calcification and Histoplasmin Sensitivity**
P. GREEN. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **63**, 143–146, Aug., 1950. 3 figs., 18 refs.

2490. **Unilateral Paralysis of the Diaphragm and Larynx associated with Inflammatory Lung Disease**
B. FREEDMAN. *Thorax* [*Thorax*] **5**, 169–182, June, 1950. 13 figs., 12 refs.

An account is given of 6 cases of pneumonia with ipsilateral paralysis of the diaphragm encountered at St. Giles's and Dulwich Hospitals during the past 3 years. In one case there was also a recurrent laryngeal palsy on the side of the inflammation.

In 2 cases the pneumonia was on the left side and in 4 on the right, the lower lobe being affected in 5 cases. In 2 patients the disease was complicated by pleural effusion, in one by dry pleurisy, and in 2 by abscess formation. In 2 cases the condition was post-operative. The onset of the paralysis seemed to coincide with the pneumonia in 2 cases, and in the others was delayed for between 4 and 6 weeks. There was no recovery for many weeks.

Of the two possible ways in which pneumonia may bring about paralysis of the ipsilateral diaphragm and

vocal cord, the author favours the theory of a toxic neuritis of the phrenic and recurrent laryngeal nerves due to exposure to an inflammatory lesion in their subpleural course. He does not consider that a diaphragmitis was responsible for the condition.

The criteria, differential diagnosis, and aetiology of unilateral diaphragmatic paralysis are discussed.

Donough O'Brien

2491. **Primary Carcinoma of the Lung**

E. A. GRAHAM. *Diseases of the Chest* [*Dis. Chest*] **18**, 1–9, July, 1950. 19 refs.

Does the increased frequency of diagnosis of carcinoma of the lung indicate a real increase in the incidence of the tumour? The author, on the basis of his experience since reporting a successful pneumonectomy in 1933 (the patient is alive and active in medical practice 16 years later), considers the increase to be real, and believes that heavy cigarette smoking over a long period is a contributory cause. He, therefore, expects that the present high consumption of tobacco among women will be reflected in an equalization of the present disparity in the incidence of squamous-cell carcinoma, which at present is far commoner among men. Adenocarcinoma, whose incidence is equal in the two sexes, seems to him to begin as an adenoma.

Bronchoscopy is positive in 60% of cases and examination of the sputum reveals malignant cells in 65% of cases. Because of earlier diagnosis, resection of the tumour has been successfully performed with increasing frequency and a lower immediate operative mortality in recent years. In all, thoracotomy has been performed by the author in 40% of cases. Pneumonectomy was possible in only 25% of cases in which the diagnosis was made, but the 5-year survival rate is 28%. The immediate post-operative mortality was 8·4% of the 139 operated upon between 1945 and 1949. Palliative resection was rarely possible, and when possible was very disappointing in its effect.

[Operation figures are recognized as a very uncertain basis for discussion, but this report of the lengthy experience of a single surgeon reflects the increasing hopefulness with which we can view the treatment of this tumour, provided the diagnosis is kept well in mind by those who, in practice, are the first to encounter a case of carcinoma of the lung.] *J. Robertson Sinton*

2492. **Bilateral Alveolar Lung Carcinoma, associated with the Injection of Thorotrast**

L. ABRAHAMSON, M. H. O'CONNOR, and M. L. ABRAHAMSON. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] **6**, 229–235, May, 1950. 12 figs., 23 refs.

A case is described in which there was widespread carcinomatous change in both lungs. The tumour was columnar-celled and mucus-secreting, the neoplastic epithelium lining the alveoli and being sometimes papillary. There was no evidence that the growth was obviously multicentric. The authors regard the case as one of alveolar carcinoma. Like other tumours which have been described it was slow-growing and showed little metastatic tendency. (There was growth in a few small lymph nodes, and a small metastasis in the pancreas.) [The authors are on very controversial ground in ascribing the origin of the growth to thorotrast injection 16 years earlier. Thorotrast was found in the liver and spleen but not in the lung.] *D. M. Pryce*

2493. **Tobacco Smoking as a Possible Etiologic Factor in Bronchiogenic Carcinoma. A Study of Six Hundred and Eighty-Four Proved Cases**

E. L. WYNDER and E. A. GRAHAM. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 329–336, May 27, 1950. 6 figs., 14 refs.

Impressed by the increased incidence of bronchial carcinoma the authors investigated factors which might play some part in this increase; their findings in respect of tobacco smoking are important. They designed a special questionary and by a series of careful controls appear to have eliminated possible personal bias; in all, 684 patients with proven bronchial carcinoma and 780 controls were examined.

The main increase has been in squamous and undifferentiated growth. Adenocarcinomata are separated because the possible role of tobacco is less definite; there were 39 men and 13 women with this type of tumour. The over-all sex ratio is 17 : 1 and, as would be expected, there are far fewer " heavy " and " excessive " smokers among the females. Of 605 males with squamous and undifferentiated carcinoma, 86·4 (54·7)% and 51·2 (19·1)% are classed as " heavy to chain " and " excessive to chain " smokers (control figures in brackets): non-smokers total 1·3 (14·6)%. The authors wisely emphasize that tobacco is only one factor, but conclude that its importance is statistically significant. They point out a lag between many years of smoking and the appearance of growth, that no less than 98·7% of cigarette smokers in the cancer group " inhaled consciously ", and that it is rare to find such a tumour in a male who has not been at least a moderately heavy smoker for many years (96% for over 20 years). Cigar and pipe smokers appear to be less at risk.

Maxwell Telling

2494. **Cancer and Tobacco Smoking**

M. L. LEVIN, H. GOLDSTEIN, and P. R. GERHARDT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 336–344, May 27, 1950. 6 figs., 2 refs.

This preliminary report suggests that among the hospital population studied there is a causal relation between cigarette and pipe smoking and cancer of the lung and lip respectively, which depends upon the type of smoking rather than upon the actual amount smoked. Over 80% of the patients studied were smokers. More than twice as many lung cancers were found among the cigarette smokers of 25 years' duration as among any of the other groups. The study is being continued.

Maxwell Telling

2495. **Primary Carcinoma of the Lung. A Clinical Study of 1205 Cases**

I. M. ARIEL, E. E. AVERY, L. KANTER, J. R. HEAD, and H. T. LANGSTON. *Cancer* [*Cancer*] **3**, 229–239, March, 1950. 7 figs., 46 refs.

Digestive Disorders

2496. **Atrophy of the Gastric Glands Produced by Beta Rays. Histological Findings in Animals**
D. M. DOUGLAS, W. R. GHENT, and S. ROWLANDS. *Lancet* [*Lancet*] **1**, 1035–1038, June 3, 1950. 8 figs., 2 refs.

This is a report of a successful attempt to reduce the secretory function of the stomach. The 4 dogs used in the experiments were made to swallow a specially-constructed apparatus consisting of three balloons superimposed outside each other.

Before the final vulcanization a mixture of 75 millicuries of P^{32} with latex was distributed evenly between the inner and middle balloons. After the apparatus had been swallowed the balloon was inflated with barium emulsion, and its position in the stomach checked radiographically. It was then left in position for between 5 and 9 hours. Biopsy specimens of the stomach were taken 39 to 75 days after this β-ray irradiation. The specimens from all 4 dogs showed atrophy of the tubular glands and an increase in fibrous tissue.

Counts of epithelial cells per high-power field showed the lowest values in the specimen examined 39 days after irradiation, with an increase in the counts from specimens examined later. The muscularis and submucosa were normal. *John Naish*

2497. **Clinical and Radiological Studies of Dilatation of the Stomach.** (Klinisch-röntgenologische Untersuchungen über die Magendilatation)
H. BERNING. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortsch. Röntgenst.*] **73**, 165–175, June, 1950. 9 figs., bibliography.

Acute dilatation of the stomach is a common condition. It may be either mechanical or atonic. The latter group includes cases of metabolic disorder with ketonaemia (diabetic coma, post-operative conditions, vomiting, infectious diseases, inanition), peritonitis, and cases after intra-abdominal procedures or blunt abdominal trauma.

The author discusses this second group with special reference to ketonaemia. One-third of patients in diabetic coma or in the pre-comatose stage show abdominal symptoms for which no satisfactory explanation has ever been offered; in 60% of cases there is at some time a complaint of distension. Gas is seen in the atonic stomach in the radiograph, but there is no tenderness or pain on palpation and the diastase content of urine is normal. In a series of such cases radiological examination was performed immediately after beginning insulin and glucose treatment. The author's routine was to screen the recumbent patient and take a plain radiograph. The dilated stomach was often seen to fill the whole of the left upper abdomen and reach to the pelvis. If barium-meal examination was considered necessary, the barium was given by spoon or catheter. By this technique very sluggish peristaltic movements or even complete atony could be demonstrated. Barium remained in the oesophagus for up to 30 minutes, and for as long as 20 hours in the stomach. The passage of barium through duodenum and jejunum was slow. However, there was no evidence of stenosis, particularly at the site where the duodenum is crossed by the mesenteric root. In pre-comatose patients these signs were less pronounced but were definitely present. One to two days after successful treatment the appearance of the oesophagus, stomach, duodenum, and jejunum returned to normal. Similar dilatation was found at post-mortem examination of comatose patients.

The author studied 19 cases of diabetic coma; only in 2 of them was the stomach of normal size and peristalsis normal. Fresh blood was sometimes found in the stomach and intestines of these patients without evidence of a responsible lesion. Dilatation of the stomach was sometimes associated with extreme dilatation of the bladder. The author considers that acidosis is responsible for central vagus paralysis and that this is the cause of the observed dilatation. Ketone bodies themselves are said to stimulate peristalsis in experiments on rabbits. Similar dilatation of the stomach was also observed in vomiting in children and in post-operative disturbance of carbohydrate metabolism. *W. J. Czyzewski*

2498. **Acidity and Ulceration. Direct Studies of the Gastric *p*H in Cases of Peptic Ulcer.** (Azidität und Ulkus. Untersuchungen am ulkuskranken Magen mit der *p*H-Sonde)
H. KREITNER. *Wiener Klinische Wochenschrift* [*Wien. klin. Wschr.*] **62**, 422–427, June 16, 1950. 6 figs., 43 refs.

For various reasons *p*H readings have not replaced titration in the analysis of the gastric contents despite their convenience. A decinormal solution of acid, that is, 100 clinical units, is equal to a *p*H of 1, a centinormal to a *p*H of 2, a millinormal to a *p*H of 3, and so on. Clinicians who use test-meals for diagnostic purposes refuse to learn new tricks and dislike change; *p*H readings are less accurate than titrations in the range of 80 to 140 clinical units characteristic of the hypersecreting duodenal-ulcer case; and a number of cases of Addisonian anaemia are associated with a fall in *p*H (for example, from 7 to 5), but this finding is not so satisfactory diagnostically as the hard-and-fast line of histamine achlorhydria. The author uses an intragastric antimony electrode and completes his circuit with a wick soaked in saturated potassium chloride, which makes the connexion with the calomel electrode (*Wien. Z. inn. Med.*, 1949, **39**, 161). [This type of electrode seems to be unpopular in England where it is believed to be inaccurate in the lower *p*H range.] Out of 20 patients with gastric ulcer gastric contents in 15 were "hyperacid", and of 40 with duodenal ulcer, contents in 39 were hyperacid. [Results are not tabulated in detail but the curves for "normal"

patients would be considered pathologically low in England and the " hyperacid " values somewhere about normal. A graph showing the effect of sodium bicarbonate, sodium trisilicate, and aluminium hydroxide is unintelligible, as the *p*H takes an hour to rise after administration of bicarbonate.

The theoretical cause of unreliability of an intragastric glass electrode is " poisoning " of the surface of the glass with mucin. After considerable trouble, the abstracter failed to find anyone in England with first-hand experience of the intragastric antimony electrode. At present Kreitner's results do not agree with English experience; it is a pity that his 3 papers have been taken up mainly with discussion and that the actual findings are never given in detail.] *Denys Jennings*

2499. **Relation of Pancreatic Secretion to Peptic Ulcer. II. Effect of Hypoglycemia with and without Pancreatectomy**
E. J. POTH, S. M. FROMM, R. DEYOUNG, and M. ALDRIDGE. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **74**, 514–518, July, 1950. 4 figs., 6 refs.

The authors state that " when the alkaline pancreatic secretions are deviated from the duodenum by external pancreatic fistula, duct ligation, or transplantation, peptic ulcers develop spontaneously. However, if the duodenum is deprived of the alkaline external secretions by means of pancreatectomy, ulcers form spontaneously only rarely ". They had suggested (*Surgery*, 1948, **24**, 62) that this difference might be attributable to a depressant effect of hyperglycaemia on gastric secretion. To clarify this problem, hypoglycaemia was produced by giving protamine zinc insulin to two groups of dogs, one normal and the other pancreatectomized. The incidence of ulcer (50%) was the same in each group. [No details are given of the type of ulcer (acute or chronic) observed.] The authors discuss the fact that peptic ulceration is rare in patients with islet-cell tumours and hypoglycaemia.
R. A. Gregory

2500. **Prolapse of the Gastric Mucosa. Report of 22 Cases**
H. G. RUDNER. *Southern Medical Journal* [*Sth. med.J.*] **43**, 480–489, June, 1950. 11 figs., 18 refs.

2501. **Chloromycetin Therapy in Chronic Ulcerative Colitis**
Z. T. BERCOVITZ. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **50**, Part 1, 2057–2060, Sept. 1, 1950.

2502. **Clinical Evaluation of Orally Administered Hog Duodenal Substance in the Treatment of Chronic Ulcerative Colitis**
M. H. STREICHER. *Gastroenterology* [*Gastroenterology*] **15**, 277–284, June, 1950. 6 refs.

The results obtained by the treatment of 43 patients suffering from chronic ulcerative colitis with hog duodenal substance (as described by Gill) are reported. The author observed all cases for 6 months before starting therapy, and adopted strict criteria of progress during the 2 years of trial. He considers that effects of a therapeutic substance are best tested on the acutely ill, and that results obtained in this group carry more weight than those obtained by treatment of milder cases.

With these criteria in mind, his results show that the substance under trial is not efficacious. The majority of mildly ill patients, however, showed some clinical improvement while under treatment. *John Naish*

2503. **The Epinephrine Test for Cortico-adrenal Reserve Function and the Excretions of Corticosteroids and 17-Ketosteroids in Chronic Ulcerative Colitis**
E. L. POSEY, D. R. MATHIESON, H. L. MASON, and J. A. BARGEN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **219**, 651–656, June, 1950.

2504. **Clinical Observations on the Severity of Liver Failure in Portal Cirrhosis**
W. E. RICKETTS, J. B. KIRSNER, and W. L. PALMER. *Gastroenterology* [*Gastroenterology*] **15**, 245–256, June, 1950. 4 figs., bibliography.

An analysis was made of 50 unselected cases of portal cirrhosis, with special reference to hepatic failure and the effects of medical treatment. The series was equally divided as to sex (an unusual finding) and included 2 children, aged 9 and 14 years. There was a history of alcoholism in 38 cases. Age, sex, and alcoholism seemed to have no bearing on the onset of hepatic failure. A nutritious diet was given, with 6 g. of choline daily in every case. As appetite improved the daily protein intake was raised to 120 to 150 g.

There were 10 deaths, 5 from hepatic failure, 4 from haemorrhage, and 1 from a combination of both causes. Satisfactory improvement followed treatment in by far the majority of cases, and signs of hepatic failure had disappeared in 32 of the 35 patients surviving at the time of the authors' report.

It is concluded from the observations that portal cirrhosis is not necessarily a progressive disease.
J. W. McNee

2505. **Prognosis of Chronic Hepatitis in Children**
G. B. LOGAN. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **25**, 299–304, May 24, 1950. 1 fig., 8 refs.

The author has studied 74 cases of chronic non-specific disease of the liver in children under the age of 14 years seen at the Mayo Clinic during the last 27 years. He prefers the term " chronic hepatitis " to " juvenile cirrhosis " in designating such cases, the latter implying an inevitable deterioration which does not necessarily occur. The diagnosis in all cases rested upon both clinical and laboratory evidence and, in an unspecified number, also upon biopsy or inspection at operation. The age at onset of symptoms was unaffected by sex and was between 0 and 1 years in 10%, 2 to 4 years in 12%, 5 to 9 years in 31%, and 10 to 14 years in 47%. At the time of this report at least 53 of the children were known to have died, 75% of them within 5 years of the onset of symptoms, but 8% only after 10 or more years. Interesting clinical details are given of the 7 patients

known to be still alive up to 21 years after the onset of symptoms and of a patient who died at the age of 30 after 23 years of recurrent haematemesis and melaena. The author has gained the impression that chronic hepatitis in children may be a reversible process, but admits that longer observation is necessary before a definite conclusion may be drawn. *R. B. Terry*

2506. **Presence of Secretin in Cystic Fibrosis of the Pancreas**

G. E. Gibbs and L. L. Gershbein. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.. N.Y.*] **74**, 336–337, June, 1950. 5 refs.

The amount of secretin present in the upper 3 feet (90 cm.) of jejunum was estimated post mortem in 4 children dying of cystic fibrosis of the pancreas and in 11 children dying of other diseases. Each jejunal specimen was extracted with 0·4% hydrochloric acid, the extract saturated with sodium chloride, and the precipitate then treated with trichloroacetic acid. The secretin content of the resulting concentrate was then assayed in dogs by the method of Gershbein, Wang, and Ivy (*Proc. Soc. exp. Biol., N.Y.*, 1949, **70**, 516). The secretin values so found in the children dying of cystic fibrosis of the pancreas fell within the normal range, as represented by the values found in the controls. *John Naish*

2507. **Functioning Acinous Cell Carcinoma of the Pancreas Accompanied with Widespread Focal Fat Necrosis**

R. R. Osborne. *Archives of Internal Medicine* [*Arch. intern. Med.*] **85**, 933–943, June, 1950. 5 figs., 8 refs.

The history is described of a white man, aged 59, admitted to hospital complaining of painful nodules in the fingers, skin of the right thigh, and the toes. The past history was not relevant. On examination, a round, smooth, slightly tender mass extending 10 cm. below the costal margin was found. The distal interphalangeal joint of the right thumb was swollen, red, and tender, as were the distal joints of both big toes. There was a round, raised swelling behind the right external malleolus, and two small, firm, tender nodules were present on the inner aspect of the right thigh; these were not attached to the skin or to deep structures. The erythrocyte sedimentation rate varied from 18 to 37 mm. in one hour. Blood count was normal except for slight eosinophilia. Urine contained albumin, a few erythrocytes, and casts. Results of all other laboratory tests, including renal and liver function tests, were normal. Radiographs of the chest showed increased hilar shadows and some opacity at the right base; the right side of the diaphragm was raised. The appearance of a biopsy specimen of one of the skin nodules resembled that in febrile, relapsing, nodular panniculitis or atypical erythema nodosum. Deep *x*-ray therapy was given to the abdominal mass, which was thought to be due to Hodgkin's disease. The patient went steadily downhill, more and more skin nodules appearing, his weight decreasing, and his temperature rising. He was readmitted covered in nodules. The right interphalangeal joint of his third finger now resembled a joint affected with rheumatoid arthritis. In addition to his slight eosinophilia he now had mild polymorphonuclear leucocytosis. The abdominal tumour was slightly larger. Treatment with penicillin, dihydrostreptomycin, and diphenhydramine ("benadryl") was unsuccessful and the patient died 4 months after his first admission.

At necropsy innumerable areas of fat necrosis were found throughout the subcutaneous fat. The region of the pancreas was occupied by an irregular mass, measuring $24 \times 8 \times 7$ cm., extending from the duodenum to the left postero-lateral chest wall and attached to the middle part of the body of the pancreas for a distance of 3 cm. The rest of the pancreas and its ducts were normal. There were several metastases in the falciform ligament in the porta hepatis, and in the coeliac axis, the liver, and the pelvic peritoneum. The primary and secondary tumours showed areas of haemorrhage and necrosis. The left kidney was totally infarcted because of an arterial thrombus in the renal artery. Both iliac veins and most of the leg veins contained ante-mortem thrombi. Histologically, the tumour consisted of polyhedral cells with large vesicular nuclei and one or two nucleoli. The stroma was delicate and contained many blood vessels; in places the tissue mimicked normal pancreatic tissue. Zymogen granules were present in many of the tumour cells. The diagnosis is discussed and the findings are compared with those in four other, almost identical, cases reported in the literature.

Walter H. H. Merivale

2508. **Fatty Change and Cirrhosis of the Liver in Patients with Pancreatic Lithiasis**

S. Sanes, D. K. Miller, F. W. Brason, and O. B. Geist. *Archives of Internal Medicine* [*Arch. intern. Med.*] **85**, 980–997, June, 1950. 8 figs., 16 refs.

Clinical histories, laboratory findings during life, and necropsy reports are given of 4 women and 3 men in whom pancreatic lithiasis was associated with pathological changes in the liver. The patients were divided into three groups. In group 1, consisting of 3 women, there was atrophy and fibrosis of the pancreas with loss of normal architecture, dilatation of the ducts, and lithiasis; the liver was enlarged and showed hypertrophic cirrhosis with gross fatty change and regeneration of bile-duct epithelium. Group 2 consisted of one case with pancreatic changes similar to those in group 1; the liver showed periportal fibrosis, but retained much of its normal structure; there was, however, distinct peripheral lobular fatty change and regeneration of bile-duct epithelium. In group 3, containing 2 women and 1 man, the pancreatic lesions were the same as in the other cases, but the liver showed only portal cirrhosis with little fatty change. The literature on animal experiments in which the effect of absent or reduced pancreatic function on the liver was studied and on human cases of associated pancreatic and hepatic lesions is reviewed. The authors sound a warning against drawing too close a parallel between the results of animal experiments and the findings in human disease, and regard the role of the pancreas in the aetiology of hepatic fatty change and cirrhosis in human subjects as not yet clarified. *Walter H. H. Merivale*

Endocrine Disorders

2509. **The Effects of the Hypophysis, Thyroid, Sex Steroids, and the Adrenal Cortex upon Granulation Tissue**
M. TAUBENHAUS and G. D. AMROMIN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 7–18, July, 1950. 7 figs., 19 refs.

An attempt is made to analyse the separate influences of the anterior pituitary, thyroid, adrenal cortical hormones, and sex steroids upon the structure of granulation tissue. In Sprague–Dawley rats, 160 to 200 g. in weight, abscess formation was induced near the right scapula by the subcutaneous injection of 0·5 ml. of turpentine *U.S.P.* The abscesses were removed on the 4th, 5th, or 6th day and fixed in 4% formalin. Histological sections were stained with haematoxylin and eosin and with Masson stain.

After hypophysectomy, the rats failed to develop the amount of granulation tissue observed in normal animals. Injection of 100- and 500-μg. doses of a purified preparation of growth hormone (contaminated with a small amount of thyrotrophin and adrenocorticotrophin) into hypophysectomized rats produced thicker granulation tissue and abundant collagen; this was particularly true of the higher dose. This effect was also seen in intact animals given 100 μg., but the higher dose actually caused some suppression of response in these animals.

In thyroidectomized animals myxoedema developed in the tissues studied, with some suppression of abscess granulation tissue. The administration of thyroxine to hypophysectomized animals stimulated the production of granulation tissue, indicating that the thyrotrophic hormone also plays a part in the stimulatory mechanism. The sex hormones (testosterone propionate and oestradiol dipropionate) inhibited granulation-tissue formation in intact animals, but stimulation occurred in some cases if a small dose of growth hormone was given at the same time. This was taken to indicate inhibition of the anterior pituitary by the sex hormones.

The adrenal cortex exerted an effect in two ways. Deoxycortone in intact animals profoundly stimulated the formation of fibroblasts, while cortisone inhibited fibroblast appearance and collagen formation and caused the appearance of large numbers of macrophages. Adrenocorticotrophin produced changes similar to those with cortisone, but less marked.

Administration of growth hormone to adrenalectomized animals had no apparent stimulatory effect; the authors can give no explanation of this phenomenon.

N. R. W. Taylor

2510. **Body Weight in Graves's Disease**
H. CONWAY. *British Medical Journal* [*Brit. med. J.*] **2**, 84–86, July 8, 1950. 2 figs., 5 refs.

The nutritional state of 47 women and 3 men with uncomplicated Graves's disease was studied, the following being determined in each case: basal metabolic rate (B.M.R.), weight on admission (expressed as a percentage of the expected weight obtained from age, height, and sex tables), calorie value of the diet for the period immediately preceding admission, and estimated daily calorie requirement. Seven patients were heavier, and 33 lighter, than their expected weight, the remaining 10 being close to it. There was no correlation between alteration in weight and the level of the B.M.R. Six of the 7 overweight patients were under 30 years of age; on the other hand, all patients over 45 were markedly underweight. Five patients whose weight was 76% or less of the expected weight had a negative daily balance of more than 1,500 Calories, although 2 women, aged 23 and 25, who appeared definitely plump (120% and 117% of expected weight) had a positive balance (1,850 and 1,600 Calories). These 2 patients responded well to methylthiouracil, their weight, calorie intake, and appetite (which had been ravenous) returning to normal. In the author's opinion, appetite is specifically influenced by thyrotoxicosis, and increase in food intake may overcompensate for the increase in B.M.R., but no fundamental distinction need be drawn between those patients who have gained weight and those who have lost.

H. McC. Giles

2511. **Thyrotoxicosis Factitia Masked as Heart Disease**
M. M. BORTIN and S. B. YOHALEM. *American Heart Journal* [*Amer. Heart J.*] **39**, 894–899, June, 1950. 2 figs., 33 refs.

A patient with auricular flutter of doubtful aetiology was shown, by the administration of radioactive iodine, to have an abnormally high rate of iodine excretion, suggesting a diagnosis either of myxoedema or factitious thyrotoxicosis. He then admitted to taking 20 grains (1·3 g.) of thyroid daily. The frequency and diagnosis of cardiac irregularities due to thyroid medication are discussed.

D. Verel

2512. **Evaluation of Agents with Thyroxine-inhibiting Effects**
S. B. BARKER, C. E. KIELY, H. B. DIRKS, H. M. KLITGAARD, S. C. WANG, and S. WAWZONEK. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **99**, 202–214, June, 1950. 14 refs.

The following tests were used in evaluating the thyroxine-inhibiting effect of certain compounds known, or suspected, to have such properties: (1) effect on the basal metabolic rate (B.M.R.) of normal rats; (2) effect on thyroxine-stimulated B.M.R. of thyroidectomized rats; (3) effect on thyroxine-depressed response of ovariectomized and thyroidectomized rats to oestrogen. Of these tests, the first had the disadvantage that the amount of thyroxine being secreted by the thyroid gland was unknown and it was therefore not possible to establish any relationship between the dose of thyroxine-

inhibitor producing a given effect and the thyroxine available to the animal. In both of the other tests the amount of thyroxine available was controlled. Of a number of phenoxyacetic acids evaluated by these tests 2 : 4-diiodophenoxyacetic acid was the most potent inhibitor of thyroxine, being able to overcome the peripheral action of thyroxine at a molecular ratio of 500 to 1; 3 : 5-diiodotyrosine and 3 ; 5 dibromotyrosine had no detectable thyroxine-antagonizing effect, whereas 4-hydroxy-3: 5-diiodobenzoic acid and 4-benzyloxy-3 : 5-diiodobenzoic acid gave consistently good results. These findings may indicate that the amino-acid chain is not necessary for inhibition of thyroxine, but that the diphenyl-ether linkage is.

P. A. Nasmyth

2513. **Pseudohypoparathyroid Tetany**

H. Bakwin, W. F. Gorman, and S. R. Ziegra. *Journal of Pediatrics* [*J. Pediat.*] **36**, 567–576, May, 1950. 5 figs., 14 refs.

2514 (*a*). **Further Observations on the Potency of Oestrogens. Clinical Assessment**

P. M. F. Bishop, N. A. Richards, and D. J. Neal Smith. *Lancet* [*Lancet*] **1**, 848–850, May 6, 1950. 17 refs.

The potency of two oestrogen preparations, ethinyl oestradiol and " equine conjugated oestrogen " (" premarin ", " strogene ") was compared with that of stilboestrol by means of a technique previously described (Bishop *et al.*, *Lancet*, 1948, **2**, 764). This consisted in administering the oestrogen by mouth to amenorrhoeic women in 14-day courses and noting whether bleeding followed withdrawal within 14 days. The first course was a " sighting " dose (usually 2 mg. daily in the case of stilboestrol); depending on whether the response to the first course was positive or negative, the dose for the second course was halved or doubled (" first bracketing " dose). The dose given in the third course (" second bracketing " dose) was similarly adjusted according to the response to the previous course, and in this way a " therapeutic unit " was determined, being the mean of two daily doses, one being the highest to fail, and the other the lowest to succeed, in producing withdrawal bleeding. In general, an attempt was made first to determine the therapeutic unit of stilboestrol and subsequently, on the same patient, the therapeutic unit of one or more of the other oestrogens.

There were 62 patients in the present series, 52 with secondary and 10 with primary amenorrhoea, to whom 462 courses of oestrogen were given, 47 therapeutic units of stilboestrol, 38 of ethinyl oestradiol, and 23 of equine conjugated oestrogens being obtained. Statistical analysis of the results showed that the relative potency, that of stilboestrol being taken as unity, was 25·674 or 21·783 (according to two different methods of analysis) for ethinyl oestradiol and 0·4949 or 0·4544 for conjugated equine oestrogen, the differences being, statistically, highly significant. In the dosage necessary for the above experiments " toxicity " was not observed sufficiently often with ethinyl oestradiol or with conjugated equine oestrogen to enable any analysis to be carried out. On the other hand, in the doses necessary to check excessive uterine bleeding, both the synthetic and the natural oestrogens often gave rise to nausea and vomiting.

The reasons for the choice of oestrogen withdrawal bleeding in cases of amenorrhoea as the end-point for the assay are discussed, cogent arguments being adduced for its preference to others that have been employed, such as relief of menopausal symptoms, production of an oestrous vaginal smear, or suppression of lactation.

G. I. M. Swyer

2514 (*b*). **Activity of Some Further Synthetic Œstrogens Determined by Experiments on Rats**

G. L. M. Harmer and W. A. Broom. *Lancet* [*Lancet*] **1**, 850–851, May 6, 1950. 7 refs.

The potency of several oestrogens—ethinyl oestradiol, 7 - methyl - bis - dehydrodoisynolic acid, " premarin ", divinyl stilboestrol, and sodium stilboestrol sulphate—relative to that of stilboestrol was determined by the authors, using ovariectomized Wistar rats. The test substances were either given by stomach-tube once daily or injected subcutaneously twice daily for 3 days. Vaginal smears were made on the 4th and 5th days, cornification of all or most of the cells seen being regarded as indicating a positive response. The relative potencies of the various substances when given by the two routes were found to be as follows:

Oestrogen	By Mouth		Subcutaneously	
	Activity	P=0·95 Limits of Error	Activity	P=0·95 Limits of Error
Stilboestrol ..	100	(assumed)	100	(assumed)
Hexoestrol ..	10	8·5–11·7	66	64–68
Dienoestrol ..	68	63–73	28	27–29
Potassium hexoestrol sulphate ..	7·3	6·7–8·0	0·98	0·91–1·05
7 - Methyl - bis - dehydrodoisynolic acid	500	445–560	46	41–51
Oestrone	2	1·6–2·4	29	28–30
Premarin	5	—	8	—
Ethinyl oestradiol..	18	14–23	233	191–285
Divinyl stilboestrol	103	75–142	45	22–91

The most notable feature of these results is that whereas ethinyl oestradiol and 7-methyl-bis-dehydrodoisynolic acid were respectively one-fifth and five times as active by mouth as stilboestrol when tested in ovariectomized rats, they were twenty times and one-fifth as active respectively, when tested in human subjects (see Abstract 2514 (*a*)). It is pointed out that this is of serious import to the research worker looking for new synthetic oestrogens, since clinically useful substances may have been discarded because of unfavourable results with test animals, while on the other hand substances found to be potent on the basis of animal tests may unwarrantably have been assumed to be similarly active in the human patient. It thus seems clear that the value of any new oestrogen can, at present, be established only by clinical test, and there is an urgent need for some reliable, but less time-consuming, technique of assay.

G. I. M. Swyer

2515. **The Effect of Diethylstilbestrol on the Calcium, Phosphorus and Nitrogen Metabolism of Prostatic Carcinoma**

A. SCHILLING and D. LASZLO. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 918–924, July, 1950. 2 figs., 16 refs.

The metabolism of a patient with diffuse osseous metastases from a carcinoma of the prostate was studied before and during 4 months' oestrogen therapy at the Montefiore Hospital, New York. Urinary and faecal excretion of calcium, abnormally high before, decreased during therapy, and the calcium balance changed from negative to positive. The serum acid-phosphatase level fell markedly; the serum alkaline-phosphatase level rose slightly. Nitrogen and phosphorus metabolism was little affected. The theoretical phosphorus balance, based on a nitrogen/phosphorus ratio of 15 : 1 and a calcium/phosphorus ratio of 2·2 : 1, was calculated. Throughout the period there was retention of phosphorus, unaccountable theoretically, which was less after treatment than before. *P. Mestitz*

2516. **Ephedrine in a Screening Test for Cortisone Substitutes**

D. ABELSON and E. N. MOYES. *Lancet* [*Lancet*] **2**, 50–52, July 8, 1950. 1 fig., 11 refs.

Both adrenocorticotrophin and adrenaline act in the same way in normal people, producing an eosinopenia by stimulating the output of glucocorticoids from the adrenal cortex. In the work here reported the action of ephedrine on the adrenocortical system was tested by eosinophil counts after its administration.

The subjects of the experiment were all in-patients with pulmonary tuberculosis in a static condition, afebrile, and undergoing, or about to undergo, collapse therapy. Out of 22 subjects who received 5 minims (0·3 ml.) of 1 in 1,000 adrenaline subcutaneously, the 6 in whom the most marked eosinopenia developed were chosen, and on another day they were given 1 grain (65 mg.) of ephedrine by mouth, the eosinophils being counted 2, 4, and 6 hours later. Thirteen subjects were given distilled water by injection as a control. In the dosage used, ephedrine caused a significant eosinopenia (from −41% to −71%) in all 6 subjects tested. *F. B. Cockett*

2517. **Tumors of the Adrenal Gland**

G. F. CAHILL and M. M. MELICOW. *Journal of Urology* [*J. Urol.*] **64**, 1–25, July, 1950. 30 figs., 42 refs.

2518. **A Case of Progeronanism (Progeria of Gilford).** [In English]

W. A. MANSCHOT. *Acta Paediatrica* [*Acta paediatr., Stockh.*] **39**,158–164, 1950. 2 figs., 15 refs.

An outline of the history and post-mortem findings in a case of progero-nanism are given. The patient, a male, had shown marked signs of abnormality since the first year of his life. At 3 years of age he had a very large forehead and no hair or eyebrows; the skin over the skull was atrophic. By 10 years the face and hands were those of an old man and the nails were atrophic; his intelligence was very high. By 18 years of age pigmentation of the skin was very marked, the blood pressure was rising, and cardiac murmurs were audible in all areas. At 26 years of age he developed cardiac asthma; his nutrition was very bad, his height was 115 cm. and his weight 15·5 kg. He had a very large skull, and dry and pigmented skin. The joints were very prominent. Blood pressure was 180/120 mm. Hg. The liver was enlarged, reflexes were weak but normal; there was some albuminuria with signs of renal impairment. The genitalia were normal. His intelligence had remained unimpaired and he was a teacher of Esperanto.

The patient died 18 months later and the post-mortem findings are given in detail. The heart and arteries showed marked arteriosclerotic and atheromatous changes. There was a striking diminution in the number of eosinophilic cells in the anterior lobe of the pituitary, but the brain tissue showed no abnormality. There was a general atrophy of the subcutaneous connective and fatty tissue, of the skeleton, and of the ligaments and cartilages. The findings indicated that the condition was due to a particular form of pituitary dwarfism combined with inadequate development of tissues arising from the mesenchyme. *E. H. Johnson*

2519. **Effects of Pituitary Adrenocorticotropic Hormone (ACTH) Therapy. Electroencephalographic and Neuropsychiatric Changes in Fifteen Patients**

P. F. A. HOEFER and G. H. GLASER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 620–624, June 17, 1950. 3 figs., 15 refs.

The neuropsychiatric effects of the administration of adrenocorticotrophin (ACTH) were studied in 15 patients with various diseases, including rheumatoid arthritis (8), dermatomyositis (2), diffuse toxic goitre (2), schizophrenia (2), and regional ileitis (1). They received the drug 6-hourly in doses of 40 to 200 mg. a day for periods of 6 to 27 days and, in one case, of 5 months. Ten of the patients showed some degree of mental change during treatment, including euphoria in all the arthritic patients who experienced relief of pain. There was, however, also a tendency to hyperactivity, tension, and insomnia; one patient became acutely manic, while another had an episode of stupor.

The electroencephalogram was mildly abnormal in 7 patients before treatment. In 13 patients " significant changes of moderate or severe degree " appeared within 3 to 5 days of the start of treatment; they consisted of reduction of alpha-activity and the presence of waves of 3 to 7 cycles per second, random or in bursts. These effects disappeared within a week of the ending of ACTH therapy. The authors discuss various possible causal factors for the mental and electroencephalographic changes, without reaching any definite conclusion.

W. A. Cobb

See also Section Pathology, Abstract 2356.

Dermatology

2520. **The Chondrioma of Normal and Pathological Epidermis.** (Le chondriome de l'épiderme normal et des épidermes pathologiques)
M. FAVRE. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **10**, 241–262, May–June, 1950. 12 figs., 10 refs.

A description is given of the spiral mitochondrial filaments as demonstrated in normal and abnormal skin by special staining techniques. The author believes that they may play an important part in the evolution of Malpighian cells and that a knowledge of the chondrioma is necessary for the solution of certain problems in normal cytology, especially in keratogenesis, and in the interpretation of the mechanisms of modification of epidermal and Malpighian cells in pathological conditions.

James Marshall

2521. **Dermatitis Caused by DDT**
L. HOLLANDER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 66–68, July, 1950. 5 refs.

2522. **Diiodohydroxyquinoline in Dermatologic Therapy**
W. LEIFER and K. STEINER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 46–53, July, 1950. 27 refs.

Diiodohydroxyquinoline was well tolerated in a lotion or ointment in a strength of 3%, and was effective in the treatment of pyodermia. One case of sensitization was observed in 70 patients who received the drug, and 6 others complained of irritation due to the drug.

John T. Ingram

2523. **Oral Administration of Aureomycin in the Treatment of Certain Dermatoses**
J. L. GRUND. *New England Journal of Medicine* [*New Engl. J. Med.*] **242**, 928–930, June 15, 1950. 7 refs.

Aureomycin was used in the treatment of certain skin conditions which had resisted orthodox measures, 500 mg. being given orally every 4 hours with food (2·5 to 3 g. daily). No local treatment was given. If improvement occurred it was usually within one week and the dosage was then reduced to 1 to 1·25 g. daily and at the end of 2 weeks to 0·5 g. daily. It was not found necessary to stop treatment on account of side-effects, although nausea and the frequent passage of loose stools occurred in many patients until the daily dose was reduced to 1 g.

Aureomycin was found to be of no value in chronic discoid lupus erythematosus (3 patients), localized herpes simplex (2 patients) and dyshidrotic eczematoid dermatitis (3 patients). Good results were obtained in 2 out of 3 patients with bullous erythema multiforme, 9 patients with sycosis vulgaris, one patient with lupoid sycosis, 4 patients with dermatitis herpetiformis, and 6 with the Darier–Ravaut–Ramel type of seborrhoeic dermatitis. These good results were maintained with a single daily dose of 250 mg. up to 7 months after treatment started.

[The author gives no indication of how long he proposes to continue treatment with a maintenance dose, nor of the prognosis after cessation of treatment.]

S. T. Anning

2524. **Ringworm of the Scalp Due to *Microsporum audouini***
A. J. E. BARLOW, F. W. CHATTAWAY, and C. S. WHEWELL. *British Journal of Dermatology and Syphilis* [*Brit. J. Derm. Syph.*] **62**, 251–261, June, 1950. 21 refs.

The recent literature concerning the local treatment of ringworm of the scalp due to *Microsporum audouini* is surveyed and the problems involved are discussed. An account is given of an epidemic in which a number of different fungicides contained in several different bases were used without *x*-ray epilation. In a total of 261 cases an average cure rate of 64% was obtained, the most effective agent being cuprammonium hydroxide in " carbowax " (67 cured out of 92 treated). The incidence of inflammatory reactions with each agent is given and the significance of these and other factors in the assessment of the value of the different local treatments discussed. The necessity for routine examination with Wood's light, checked if deemed clinically necessary by microscopical examination, is emphasized.

G. B. Mitchell-Heggs

2525. **Treatment of Tinea Capitis with Estrogenic Hormones**
W. L. DOBES. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 58–65, July, 1950. 8 refs.

Administration of diethylstilboestrol by injection to 13 patients with *Microsporum audouini* infection of the scalp did not effect a cure, but in 6 cases it loosened hair so that manual epilation was facilitated. The treatment is suitable only for males. *John T. Ingram*

2526. **So-Called " Lupus Erythematosus Inclusion Phenomenon " of Bone Marrow and Blood. Morphologic and Serologic Studies**
L. BERGMAN, A. R. AXELROD, H. L. GOODMAN, and R. I. MCCLAUGHRY. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 403–418, May, 1950. 24 refs.

Changes in the bone marrow which were regarded as characteristic of lupus erythematosus disseminatus (L.E.D.) were first described from the Mayo clinic by Hargraves, Richmond, and Morton in 1948. The present authors have confirmed and extended these findings, and made some studies of the pathogenesis of the disease.

The phenomenon consists in the appearance within neutrophil polymorphonuclears and band forms, and rarely within other cells, of round homogeneous Feulgen-positive bodies, usually basophilic, which are almost certainly the result of nuclear breakdown, probably from lymphocytes. The characteristic cells are not seen in direct smears, but only after heparinization and centrifuging. Small numbers of free bodies are found in direct smears, but formation of bodies and their phagocytosis are greatly accelerated by centrifuging. The cells of normal marrow mixed with plasma from a patient with L.E.D. show the same change. It is probable that these characteristic bodies seen in the marrow are related to the basophilic masses seen in the vicinity of granulomatous lesions in cases of L.E.D., though the present authors have been unable to confirm the Unna-Pappenheim effect which Klemperer, Gueft and Lee have recently used as evidence for their theory that these masses consist of depolymerized desoxyribose nucleic acid.

Points of special importance in the present paper are the following. (*a*) The change was seen in all of 4 cases of acute L.E.D., and in none of 8 cases of other collagen diseases. (*b*) The change was seen in 6 cases (out of an unspecified total) in which L.E.D. was probably not present, but more than ten affected cells per 500 neutrophils (band forms and polymorphonuclears) in the marrow smears were never seen except in acute L.E.D. (*c*) Rapid recognition of the bodies is helped by fixation of wet smears in methyl alcohol and by Papanicolaou staining. (*d*) The production of the change in normal marrow cells by L.E.D. plasma may afford an additional and truly specific test for the disease. (*e*) There is considerable quantitative variation in the reaction of different specimens of marrow, especially from patients with various unrelated diseases, to L.E.D. plasma. (*f*) Rodent and opossum marrow also reacted to L.E.D. plasma. (*g*) The activity of the plasma is in the gamma globulin fraction. *Bernard Lennox*

2527. **The Use of Testosterone in Chronic Lupus Erythematosus**

J. L. FROMER. *Lahey Clinic Bulletin* [*Lahey Clin. Bull.*] 7, 13–17, July, 1950. 2 refs.

Since August, 1949, testosterone has been given at the Lahey Clinic, Boston, to 23 patients with chronic lupus erythematosus. Their ages varied from 14 to 64 years, the duration of disease from 4 months to 6 years. There were 10 males and 13 females in the series. Of the 23 cases, 19 were of the chronic discoid form of classical type, with lesions on scalp, face, and neck. Four cases were of the chronic disseminated type, with lesions on the limbs, upper chest, or abdomen.

Three types of therapy were used: (1) injection of testosterone propionate; (2) methyltestosterone transmucosally; (3) crystalline-free testosterone transmucosally. Regardless of sex, the initial dose was 20 mg. of methyltestosterone or 8 g. of crystalline-free testosterone. Patients who received testosterone by injection were given 50 mg. intramuscularly, and in some cases 100 mg. A dose of 20 mg. was considered to be the basic dose by the transmucosal method. None was given by the oral route. If no clinical improvement followed this basic dosage after 4 to 6 weeks the dose was increased by increments of 10 mg., so that ultimately 40% of the patients were taking 50 mg. of methyltestosterone or its equivalent.

The effect of administration of the substance in some of the cases was dramatic. Of the 23 patients, 5 have had complete remissions and now show only mild skin atrophy and residual pigmentation. In 11 of the cases there was a distinct improvement in the skin lesions, but in 7 cases there was no change. In 3 cases in which treatment was discontinued for 2 to 3 weeks, skin lesions recurred. No masculinization occurred in females nor was any change of libido seen in normal males.

The author suggests that testosterone may have effects on enzyme systems or cellular metabolism, or cause immunological changes. He completes his paper by describing in detail the management of a case of discoid lupus erythematosus. *H. S. Laird*

2528. **A New Method for the Treatment of Epitheliomata with Podophyllin.** (Une nouvelle méthode de traitement des épithéliomas: la podophyllinothérapie (peltacure))

F. WYSS-CHODAT. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 647–651, June 24, 1950. 28 figs., 2 refs.

Sullivan and other workers have shown that podophyllin inhibits mitosis. This is a preliminary report of the results of treatment of different types of skin lesion by local application of podophyllin. Depending on the amount of infiltration and ulceration, either an ointment or a solution of podophyllin in alcohol or in oil is used.

Details of treatment with photographs of the macroscopical and microscopical appearance of the lesion are given. Cases in which there was marked improvement and cure were of basal-cell epitheliomata (7), squamous-cell epithelioma arising on lupus vulgaris (1), fibrous pigmented naevus (1), and pigmented soft mole (1). It is probable that the podophyllin has a direct action on the mitotic cell. *H. R. Vickers*

2529. **Resin of Podophyllum in Treatment of Cancerous and Precancerous Conditions of Skin. Effect on Basal Cell Epithelioma and Seborrheic, Senile and Radiation Keratoses**

L. M. SMITH and H. D. GARRETT. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **61**, 946–956, June, 1950. 4 figs., 7 refs.

Encouraged by the results of treatment of seborrhoeic keratoses by repeated applications of 30% resin of podophyllum in mineral oil, the authors treated a patient with multiple superficial epitheliomatosis in the same way, obtaining a good clinical result. More recently, cases of basal-cell epithelioma and seborrhoeic, actinic, and *x*-ray keratosis have been treated, and a preliminary report is given of the results. Later, 20% resin of podophyllum in compound tincture of benzoin was used. The substance was applied under an occlusive dressing, with protection of the surrounding skin, and the dressing changed daily or every 2 or 3 days, the necrotic tissue being removed at each change of dressing. There was some inflammatory reaction, at times painful. Great

care must be taken to see that no resin touches the eyes. Microscopical studies seemed to show a selective action on the diseased epithelial cells.

[In the subsequent discussion, the use of the resin in treating squamous-cell carcinoma, cutaneous horns, and molluscum contagiosum was mentioned, and the opinions expressed appear to indicate that this method of treatment is worthy of further trial and study.]

J. E. M. Wigley

2530. **Calcified Skin Epitheliomata.** (Epiteliomas calcificados de la piel)

N. PUENTE DUANY. *Boletín de la Sociedad Cubana de Dermatología y Sifilografía* [*Bol. Soc. cubana Derm. Sif.*] **7**, 45–113, June, 1950. 18 figs., bibliography.

Five cases of the rare tumour, calcified skin epithelioma, were seen in a series of 2,000 epitheliomata; as with other epitheliomata, 45% are found on the head and face, but these tumours are more frequent in young people. Generally small and comparatively benign, they consist of two parts: the epithelial part, which has a marked tendency to keratinization; and the vascular stroma, which remains inactive in the region of the actively growing epithelial islands but proliferates around the keratinized areas. Calcification and ossification are generally, but not always, associated with slow growth of tumours. It is considered that the "necrosis" mentioned by some authors is actually the keratinized epithelium in which the nuclei stain with eosin. The histogenesis is discussed, and an origin from the hair follicles is suggested. *George Hickie*

2531. **Pathogenesis and Treatment of Scleroderma and Related Clinical Conditions.** (Zur Pathogenese und zur Therapie der Sklerodermie und ihr verwandter Krankheitsbilder)

R. EMMRICH and H. ZUR HORST-MEYER. *Zeitschrift für Klinische Medizin* [*Z. klin. Med.*] **146**, 578–592, 1950. 21 refs.

The findings in 6 cases of scleroderma, 1 of acrodermatitis atrophicans, 2 of scleroedema, and one of dermatomyositis are discussed. The fact that scleroderma is not a purely local skin condition but part of some general disturbance is shown in the blood picture and chemistry. There is a mild polymorphonuclear leucocytosis and raised erythrocyte sedimentation rate in most cases. The total protein content of the serum is within normal limits, but in all cases there is a tendency to reversal of the albumin–globulin ratio, with an increase particularly in the γ-globulin fraction. Foci of infection were present in all cases: in teeth, tonsils, gall-bladder, etc. This is considered to be an important aetiological factor, another being the oedema which precedes the actual hardening of the skin. The vegetative nervous system is known to play an important part in the changes in blood supply and vascular permeability which lead to this oedema. The scleroproteins are thought to be derived from the proteins of this oedema fluid, though what physical and chemical changes they undergo in the process is not exactly understood. The reaction of the body to these abnormal scleroproteins is reflected in the blood changes which have already been referred to. There may also be secondary disturbances in mineral metabolism, the endocrine glands, and other organs.

Scleroderma is to be considered, then, as a general disturbance in protein metabolism, which links it with such other scleropathies as cirrhosis of the liver, nephrosclerosis, and arteriosclerosis. An important localizing factor in many cases of scleroderma is the presence of Raynaud's disease, but since this sometimes does not precede, but only accompanies, the scleroderma its exact significance remains obscure. Some softening of the skin and improvement in the blood picture was achieved by implantation of the anterior lobe of the pituitary of a calf in 7 of the 9 cases thus treated. The success of this operation was greatest in the early cases, but even then it could not be described as a cure. *Marianna Clark*

2532. **Hereditary Haemorrhagic Telangiectasia: a Genetic and Bibliographical Study**

H. G. GARLAND and S. T. ANNING. *British Journal of Dermatology and Syphilis* [*Brit. J. Derm. Syph.*] **62**, 289–310, July–Aug., 1950. 19 figs., bibliography.

An attempt was made to review fully the literature on hereditary haemorrhagic telangiectasia, and 244 affected families are considered. A further 20 families not reported previously are described. There is a table giving details of 112 families in which the full sibships were reported. This table shows that the proportion of affected males to females is 449 : 463, and of normal males to normal females 348 : 362. The proportion of affected to normal sibs is 766 : 851. The defect is transmitted by males and females in approximately equal proportions as a dominant character. It would seem to be relatively more common among Jews than among Gentiles, and more common in most communities than is generally realized. *John T. Ingram*

2533. **Partial Alopecia due to Scalp Massage**

R. E. BOWERS. *British Journal of Dermatology and Syphilis* [*Brit. J. Derm. Syph.*] **62**, 262–264, June, 1950. 1 fig., 4 refs.

Observation of normal infants shows that the constant friction of the head on the pillow may produce a patch of short hair on the occiput, even though the rest of the hair is growing strongly. In view of the frequency with which the public is urged to massage the scalp with one application or another, the author considers it likely that a similar condition occurs, but is usually not recognized, in adults. Six cases of patchy baldness in patients addicted to vigorous massage of the scalp are reported, in all of which regrowth of the hair occurred after discontinuing the practice. The clinical appearances resulting from vigorous massage are described and the suggestion made that some cases diagnosed as trichorrhexis nodosa and fragilitas crinium may in fact be due to massage of the scalp. *G. B. Mitchell-Heggs*

2534. **Unilateral Systematized Vitiligo.** (Vitíligo unilateral sistematizado o nevus acrómico)

T. CARO-PATÓN. *Actas Dermo-sifiliográficas* [*Act. dermo-sifiliogr., Madr.*] **41**, 717–723, May, 1950. 2 figs., 10 refs.

Venereal Diseases

2535. **The Incidence of Lymphogranuloma Venereum as Determined by the Quantitative Complement-fixation Test**
N. M. LUGER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 351–355, July, 1950. 14 refs.

During 1947–8, in a blood donor campaign, routine complement-fixation tests for lymphogranuloma venereum with " lygranum " antigen were carried out on three sections of the population of a Virginian town. Patients with a titre of 1 in 20 or over were suspected of having an active infection.

Of 365 female factory workers (negresses) 163 gave a positive result and in 77 of these the titre was 1 in 20 or over. Of 86 male factory workers tested 28 gave a positive result and in 15 the titre was 1 in 20 or above. Of 89 negro college students (women) 15 had a positive reaction, but only in 3 was the titre at or above 1 in 20, while of 89 male negro college students only 2 gave positive reactions, the titre in both cases being below 1 in 20. Thus out of 178 negro students, drawn from different educational and socio-economic strata from the factory workers and of different age-groups, only 4% had positive reactions and only 1·7% had a titre greater than 1 in 20. Out of 45 white men and 45 white women attending clinics, only 6 gave a positive reaction and only in one was the titre 1 in 40.

It has long been suspected that there is a large reservoir of active infection with lymphogranuloma venereum in the American negro; the present study confirms that suspicion. *R. R. Willcox*

2536. **Effectiveness of Antichancroidal Drugs Tested by Autoinoculation of Bubo Fluid**
R. R. WILLCOX. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 378–382, July, 1950. 1 fig., 3 refs.

Chancroid is notoriously auto-inoculable. The author inoculated 35 patients suffering from chancroid intracutaneously with 0·05 to 0·1 ml. of fluid from their own buboes, and 2 with material from their own sores; 9 were untreated and acted as controls, the remainder being given various drugs before or at the time of inoculation. In 8 of the 9 controls pustules developed, whether the " dmelcos " skin test had been positive or not. Of 11 patients treated with sulphonamides before, or simultaneously with, inoculation only one developed a positive reaction; of 2 patients who were given penicillin one had a positive reaction and the other did not; of 2 patients treated with a combination of penicillin and sulphathiazole both were protected; 2·25 g. of chloramphenicol given by mouth over a period of 3 days protected one patient, whereas 2 g. of aureomycin given by mouth over 2 days to another failed, but delayed the reaction considerably; streptomycin in doses of 1·5 to 3 g. protected 3 patients; and neoarsphenamine was only successful in 2 out of 6 cases. From these experiments it is clear that both streptomycin and the sulphonamides have a definite prophylactic action against experimental chancroid. *T. E. Osmond*

2537. **Chloramphenicol (Chloromycetin) in Experimental Syphilis of Rabbits**
O. M. GRUHZIT and R. A. FISKEN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 338–341, July, 1950. 7 refs.

A series of 53 rabbits were inoculated intratesticularly with a suspension of *Treponema pallidum* (the Nichols strain). Two groups of 10 animals were treated on the fourth day after inoculation with 25 and 37·5 mg. of chloramphenicol per kg. subcutaneously twice daily for 2 to 5 days in order to assess the prophylactic effect of the drug. Treponema-positive lesions developed between 6 and 7 weeks after inoculation, at the same rate as in 32 untreated controls.

Larger amounts of chloramphenicol (100 to 200 mg. per kg. per day, given intramuscularly in two equal doses for 2 and 4 days) in cases of early, progressing syphilis of rabbits (7 weeks) caused marked initial healing of lesions and temporary disappearance of spirochaetes, followed by recurrence of lesions or the development of syphilomata in rabbits undergoing lymph-node transfer. Prolongation of treatment from 4 to 8 days (to a total of 1,600 mg. per kg. or over) cured all of 14 rabbits with long-standing infections of 6 to 9 months' duration.

It is pointed out that the concentration of the drug in serum of rabbits is relatively low in comparison with that in human subjects. This may account for the apparent difference in therapeutic success in the two species.
R. R. Willcox

2538 (*a*). **Reinfection in Experimental Syphilis in Rabbits following Penicillin Therapy. III. Development of Immunity in Early Syphilis**
R. C. ARNOLD, R. D. WRIGHT, and S. LEVITAN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 324–326, July, 1950. 2 refs.

In order to find out at what stage of the disease immunity to syphilis develops and to determine the duration of immunity after treatment, the authors experimentally infected young male rabbits with syphilis and, 5 to 11 weeks after the disease had developed, treated them with curative doses of penicillin. During a 4-month period of observation none developed clinical signs of syphilis but, in 8 out of 22 cases, lymph-node transfer gave rise to active syphilis in other rabbits, showing that only partial immunity had developed; in the remaining 14 there appeared to be complete immunity. The time periods were as follows: after 5 weeks, 2 showed partial and 3 complete immunity; after 2 to 8 weeks the numbers were 6 and 7 respectively, and after 10 to 11 weeks, 0 and 4. These experiments, together with those reported

previously (*Amer. J. Syph.*, 1947, **31**, 264 and 489) in which animals treated with penicillin during the early weeks of the disease were successfully reinfected, suggest that immunity to syphilis increases with the duration of the disease before treatment.

T. E. Osmond

2538 (*b*). **Reinfection in Experimental Syphilis in Rabbits Following Penicillin Therapy. IV. The Development and Character of Immunity in Latent Syphilis**

R. C. ARNOLD, R. D. WRIGHT, and C. MCLEOD. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 327–330, July, 1950. 2 refs.

Continuing their previously reported experiments (see Abstract 2538 (*a*)), the authors treated 30 young male rabbits suffering from latent syphilis of 8 months' duration with sufficient penicillin to ensure cure and, 6 months later, inoculated them in the same way as for the original infection. During subsequent observation for 4 months none developed any signs of syphilis, although 8 animals died. At the end of this time lymph nodes from the 22 survivors and from one which had died after 85 days were transferred to normal rabbits, which were then observed for 4 months; 13 developed clinical syphilis and 10 remained symptom-free. The 22 rabbits which had survived reinoculation for 6 months were then adequately re-treated with penicillin and, after a further 6 months (during which 4 died), the 18 survivors were inoculated again and observed for 4 months. Of the 16 which survived 5 had developed partial and 11 complete immunity as shown by lymph-node transfer. Analysis of results in these 16 animals over the 3 years showed that 6 were free from infection and 3 had a symptomless infection after both reinoculations, while 2 were free from infection after the first and had a symptomless infection after the second reinoculation, and 5 had a symptomless infection after the first and no infection after the second reinoculation. Disregarding the booster effect of the second inoculation, the immunity which had developed during latent syphilis of 8 months' duration thus persisted for 6 to 28 months after penicillin treatment. *T. E. Osmond*

2539. **Variations of Serologic Pattern in Patients given Penicillin Therapy for Supposed Early Latent Syphilis**

E. W. THOMAS, S. LANDY, and L. DE MELLO. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 364–372, July, 1950. 2 refs.

The authors treated 127 patients, serum-positive and said to be suffering from early latent syphilis, with 3 to 4 million units of penicillin and followed them up, carrying out quantitative complement-fixation and Kahn tests, for periods of 1 to 4 or more years. The serological reactions in 22% became and remained negative, and in 7% returned to positive; in 21·3% there was a significant fall in titre to below 16, 31·5% showed titres falling but still above 16, and 10·2% showed no significant change of titre; in 8% of cases there had been agreement between the results of the two types of test before treatment, but considerable discrepancies after treatment. Of the 13 patients included above whose blood showed no change of titre, 4 or 5 probably had biological false-positive reactions, and of 14 other patients (not included) who showed marked discrepancies in results before treatment, 3 or 4 probably also gave false reactions (details of these are given in a table). Re-treatment was given to 30 patients whose blood continued to have titres between 16 and 256: 5 showed a marked fall in titre, 9 remained unchanged, and 16 have been followed up for less than 6 months.

The difficulties of interpreting positive tests in patients without symptoms are discussed: when both types of reaction are strongly positive and remain so a diagnosis of syphilis is almost certain, but when there are marked discrepancies and fluctuations apart from treatment the decision is difficult, and diagnosis must be based on the history and the findings on prolonged observation. The authors believe that all but 4 or 5 of their 127 patients had syphilis. *T. E. Osmond*

2540. **The Effect of Treatment on the Prognosis of Cardiovascular Syphilis**

C. W. BARNETT and A. A. SMALL. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 301–318, July, 1950. 1 fig., 10 refs.

Of the 334 patients with cardiovascular syphilis studied, 57 were negroes and only 50 were females; 240 had aortic regurgitation alone, 39 aneurysm alone, and 55 both lesions. They were divided into two groups, according to whether they had received more or less than 35 injections of an arsenical or bismuth preparation or both. Of 69 of the patients who were without symptoms and received little treatment, 21 were known to have died, while of 73 receiving much treatment, 15 died. Of 39 with mild heart failure receiving little treatment and 45 given much treatment, 17 and 12 died respectively, while of 43 patients with moderate or severe failure receiving little treatment, 35 died, compared with 25 out of 47 patients receiving much treatment.

In a group of 131 with symptoms followed up for more than one year the mortality rate for those receiving little treatment was 57%, whereas the rate was 40% for those receiving much treatment (standard error of difference calculated as 9%). However, 32% of those receiving much treatment obtained symptomatic relief, compared with only 13% of those given minimal treatment. On the other hand, in a group of 151 without symptoms followed up for more than one year, the proportion of deaths in the two sub-groups was 22% and 20% respectively.

The statistical difficulties in the assessment of results are discussed in full, and the published work of other workers is tabulated. It is shown that cases with and without symptoms must be separated for study, and it is concluded that treatment improves prognosis at all stages of cardiovascular syphilis, but is most effective when given before the onset of symptoms. *R. R. Willcox*

2541. **Pulmonary Arteritis due to Acquired Syphilis**

M. R. HEJTMANCIK, J. Y. BRADFIELD, and R. H. RIGDON. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 236–244, May, 1950. 5 figs., 17 refs.

Genito-urinary Disorders

2542. **Nephritis due to Kidney Auto-antibodies** (Nephritis durch Nierenautoantikörper)
E. FRICK. *Zeitschrift für Immunitätsforschung* [*Z. ImmunForsch.*] **107**, 411–417, June, 1950. 10 refs.

Rats injected, on two or three occasions separated by 2 or 3 weeks, with mixtures of killed tubercle bacilli (or old tuberculin), liquid paraffin, sterile lanolin, and 20% suspension of rat kidney lightly ground and suspended in saline develop serum antibody to rat kidney, as judged by complement-fixation tests. In association with this, they themselves show a diffuse glomerulonephritis with extensive nephrotic changes. Injection of rat-kidney suspensions with liquid paraffin and lanolin, but without killed tubercle bacilli, does not excite the production of antibodies to rat kidney in rats.

C. L. Oakley

2543. **Syndrome Characterized by Glomerulonephritis and Arthritis. Libman–Sacks Disease with Predominantly Renal Involvement**
G. W. DAUGHERTY and A. H. BAGGENSTOSS. *Archives of Internal Medicine* [*Arch. intern. Med.*] **85**, 900–923, June, 1950. 4 figs., 18 refs.

This report from the Mayo Clinic describes an unusual group of cases related to Libman–Sacks disease in which the clinical and pathological findings were so similar as to constitute a recognizable syndrome. The patients, 3 male and 4 female, were aged 17 to 41 years. The first occurrence was a transient migratory arthritis of small and medium-sized joints which left no residua. The first evidence of renal involvement was albuminuria with casts, erythrocytes, and leucocytes in the urinary deposit. This was followed by nephrotic oedema with marked albuminuria, low serum albumin levels, and increased plasma cholesterol and total lipid values. Blood pressures of 125/75 to 180/105 mm. Hg were recorded. A mitral diastolic murmur with a recurrent pericardial friction rub was heard in one case, and apical systolic murmurs were heard in 5 others. Retinal changes were seen in 3 cases. One woman had erythematous macules on her face, trunk, and thighs, another had macules on her arms and trunk, and a third urticarial lesions on her feet and ankles. Ptosis of the eyelids occurred in one case. Most patients were pyrexial and anaemic and had markedly increased erythrocyte sedimentation rates. Blood cultures were negative. After a period of massive oedema varying from 2 weeks to 10 months urinary output fell and rapidly increasing nitrogen retention was followed by death in uraemia. Necropsy was allowed in 4 cases, of which 3 showed evidence of subacute and 1 of chronic glomerulonephritis. The kidneys were large and pale. The basic lesion was proliferation of the endothelial cells of the capillary loops causing obstruction; crescent formation and wire-loop changes were also found in some cases. The heart was always enlarged; myocarditis, valvulitis, pericarditis, and arteritis were usually present. The similarity of these findings to those in glomerulonephritis, rheumatic fever, and periarteritis nodosa, which are regarded by some workers as hyperergic diseases, leads the authors to suggest that the hyperergic state may be an important factor in the Libman–Sacks syndrome.

I. Ansell

2544. **Symptomatology and Diagnosis of Thrombosis of the Renal Artery.** (К симптоматологии и диагностике тромбоза почечных артерий)
B. P. KUSHELEVSKIJ and S. S. BARATS. Клиническая Медицина [*Klin. Med., Mosk.*] **28**, No. 6, 39–45, June, 1950. 2 figs., 11 refs.

The author reviews the literature on occlusion of the renal artery. His own work is based on a study of the condition in 13 men and 8 women, aged between 24 and 70 years, in 11 of whom the left renal artery was blocked, in 9 the right, and in 2 both. In the period during which the series was collected renal-artery occlusion (confirmed post mortem) caused as many deaths as coronary occlusion in the authors' Sverdlovsk clinic. Thrombosis and embolism result either from cardiac disease or from arteriosclerosis, with an intercurrent infection such as influenza as a common precipitating cause.

The patient's general condition is one of collapse with vomiting and subsequent pyrexia, as in coronary embolism. The local signs and symptoms are those of an " acute abdomen ", with pain, reflex rigidity, and ileus. There is oliguria or, in the uncommon bilateral cases, anuria. While albumin and blood may be present in the urine, they will not be found if the affected kidney is secreting no urine at all. Frequently there is a sudden, severe rise in blood pressure, due to renal ischaemia. Hyperprothrombinaemia is present. In all cases a condition predisposing the patient to thrombosis or embolism can be found.

Jeffrey Boss

2545. **The Renal Blood Flow: Physiological, Pathological, Clinical, and Therapeutic Aspects.** (Le flux sanguin renal: aspects physiopathologiques, cliniques et thérapeutiques)
F. REUBI. *Helvetica Medica Acta* [*Helv. med. Acta*] Suppl. 26, 1–108, 1950. 23 figs., bibliography.

2546. **Bilateral Diffuse Nephrocalcinosis: Report of 2 Cases**
J. E. GERACI, H. W. HARRIS, and N. M. KEITH. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **25**, 305–315, June 7, 1950. 4 figs., 24 refs.

2547. **Present Role of the Artificial Kidney in Clinical Therapy**
J. P. MERRILL. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 100–107, July, 1950. 4 figs., 10 refs.

Disorders of the Locomotor and Osseous Systems

2548. **The Differential Sheep Cell Agglutination Test in Arthritis**
J. R. DORDICK and M. M. WASSERMAN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 526–529. June, 1950. 7 refs.

The differential sheep-cell agglutination test for rheumatoid arthritis was first described by Rose *et al.* in 1948, although, as the authors point out, Waaler in 1939 had previously demonstrated the presence, in sera from 51% of cases of rheumatoid arthritis, of a relatively thermostable activator of sheep-cell agglutinins, which was unrelated to blood-group or heterophil antibody.

By Rose's technique, the authors examined 17 sera from healthy persons, 73 from patients with non-arthritic conditions (including bacterial infections, virus pneumonia, colitis, infective hepatitis, allergic diseases, glomerulonephritis, infectious mononucleosis, thyrotoxicosis, osteomyelitis, neoplasms, and uterine and intestinal bleeding), 83 from cases of degenerative joint disease, 27 from those with miscellaneous diseases of the locomotor system, and 26 from cases of rheumatoid arthritis including spondylitis (3) and Still's disease (2).

The only positive results (titre of 1 in 16 or over) were in 13 of the 21 cases of peripheral rheumatoid arthritis, one case of degenerative joint disease, and one case out of 3 of scleroderma. The cases of Still's disease and spondylitis ankylopoietica without peripheral joint involvement gave negative results, as did also 3 cases of inactive rheumatoid arthritis, and 5 cases of active rheumatoid arthritis. " Those patients having the disease for three years or more would be more likely to exhibit a positive serologic reaction. . . . As a test for the early diagnosis of rheumatoid arthritis, its usefulness would appear to be of limited value." *E. G. L. Bywaters*

2549. **Electrophoretic Study of Plasma and Serum Proteins in Rheumatoid Arthritis. Comparison with Flocculation Reactions and other Tests.** (Estudio electroforético de las proteínas del plasma y del suero sanguíneo en la artritis reumatoidea. Su comparación con las reacciones de floculación y otras pruebas)
R. ARMAS CRUZ, M. MADRID, G. LOBO-PARGA, F. VALENZUELA, C. J. MEREDITH, and L. GOSTIN. *Revista Médica de Chile* [*Rev. méd. Chile*] **78**, 259–263, April, 1950. 2 figs., 19 refs.

Electrophoretic study of blood proteins was carried out on 25 patients with typical rheumatoid arthritis; there were no complicating factors and the patients had not received gold. The electrophoretic investigation of the plasma showed that the amount of fibrinogen was increased up to three times the normal value. The albumin concentration in serum was lowered, and the levels of all the globulins were raised. The albumin/globulin ratio was thus altered, and the authors think that these changes are of statistical significance. Similar changes were also found in plasma proteins, except that the amount of beta-globulin was not increased. The cephalin–cholesterol, thymol, and colloidal-gold flocculation tests were positive in a high percentage of cases; this finding is probably due to the increase in gamma-globulin following the appearance of antibodies. It was found that the more severe the clinical picture, the lower became the albumin/globulin ratio and the higher the content of fibrinogen and of alpha- and gamma-globulins. The authors do not consider the findings to be of any prognostic import. *Paul B. Woolley*

2550. **Cardiac Lesions in Rheumatoid Arthritis. A Summary of Recent Developments and a Bedside Study of Patients and Controls**
E. F. ROSENBERG, L. F. BISHOP, H. J. WEINTRAUB, and P. S. HENCH. *Archives of Internal Medicine* [*Arch. intern. Med.*] **85**, 751–764, May, 1950. 14 refs.

Post-mortem studies over the past 5 years have revealed an incidence of rheumatic heart disease in patients dying of rheumatoid arthritis considerably higher than that in the general population. This fact is at variance with clinical findings in patients suffering from rheumatoid arthritis.

The authors carefully examined 114 patients with rheumatoid arthritis and 33 with rheumatoid spondylitis for cardiac abnormalities at the Army Rheumatism Centre, Hot Springs, Arkansas; 100 members of the staff were examined as controls. The examination was specifically directed to a discovery of minor cardiac abnormalities, and two different observers examined each patient independently. The methods used included auscultatory, radiological, and electrocardiographic ones.

The investigation revealed that the incidence of rheumatic heart disease, judged on clinical evidence, was similar in the arthritic group and in the control group.
R. H. J. Fanthorpe

2551. **The Effect of Denervation of the Carotid Sinus in Rheumatoid Arthritis.** (Action de l'énervation sinu-carotidienne sur la polyarthrite chronique progressive)
L. J. MICHOTTE, J. BUISSERET, H. DEVESTER, G. DONEUX, and M. HORNIATCHEVSKI. *Revue du Rhumatisme* [*Rev. Rhum.*] **17**, 141–148, April, 1950.

The authors confirm a previously reported observation that denervation of the carotid sinus is followed by stimulation of the adrenal cortex. The evidence of increased adrenocortical activity consists in: (1) the appearance of a diabetogenic effect, shown by a characteristic change in the glucose tolerance curve; (2) an increase in the serum albumin/globulin ratio; (3) a diminution of at least 50% in the number of circulating eosinophils; (4) an increase in the ratio of urinary uric acid to creatinine. These effects are observed to follow injection of cortisone or of adrenocorticotrophin.

Temporary denervation was first effected by infiltration of the region of the carotid sinus with a local analgesic. The authors then decided to study the effect on the course of rheumatoid arthritis of surgical removal of the carotid body. The operation was carried out on 7 patients. One died. The other 6 showed the same dramatic improvement as that observed to follow administration of cortisone. Objective improvement in condition of the affected joints was obvious within 48 hours. The duration of the supposed adrenocortical stimulation is unknown, as also is the ultimate effect on the patients treated.

(In a discussion of the paper, Coste remarked that tests for adrenocortical stimulation are positive not only after injection of adrenaline, but also after injection of very varied substances, and the great majority of these substances have no therapeutic effect in polyarthritis. These tests, though perhaps an index of adrenocortical activity, give no information on the production by the adrenal of substances with an anti-rheumatic action.)

Kenneth Stone

2552. **Pachydermoperiostosis.** (La pachydermoperiostose)

J. VAGUE. *Annales de Médecine* [*Ann. Méd.*] **51**, 152–173, 1950. 3 figs., bibliography.

On the basis of a study of the literature and of his own observations the author reviews the syndrome of pachydermoperiostosis. This syndrome appears at puberty and develops slowly over many years; out of some 60 recorded cases only 4 have occurred in females. It consists in a thickening of the skin, affecting particularly the horny layer and accompanied by hypertrophy of the sebaceous glands, with formation of folds resembling in their contours the convolutions of the cerebral cortex. The skin of the extremities, the face, and the scalp are especially affected. There is also a thickening of the periosteal bone, most frequently in the extremities but extending in some cases to the entire skeleton. The medullary cavity of the affected bones is narrowed and on occasion obliterated. The profile of the bones is obscured and exostoses form, but there is no tendency to ankylosis. There is no evidence of any other organic lesion. The differentiation of this syndrome from acromegaly, pulmonary osteoarthropathy, and osteosclerosis is discussed and the distinctive features are established, although it is suggested that these conditions are frequently confused in the literature. The author believes that the disease is genetic in origin.

T. A. A. Hunter

2553. **Clinical Features and Pathogenesis of Marble-bone Disease.** (Zur Klinik und Pathogenese der Marmorkrankheit)

B. WEICKER and E. SCHMITZ-CLIEVER. *Zeitschrift für Klinische Medizin* [*Z. klin. Med.*] **146**, 633–643, 1950. 4 figs., 19 refs.

This article describes a family in which the father and all his 4 children, aged between 18 and 3 years, suffer from classical marble-bone disease. In the case of the father almost the whole skeleton is affected by dense osteosclerosis. In the children the disease is much less advanced and is most marked in the metaphyses nearest the knee-joints. The father suffers from bilateral secondary osteo-arthritis of the hips, but apart from that the disease is symptomless in all cases. The blood findings are very similar in all 5 patients, there being mild anaemia with anisocytosis, and slight leucocytosis with considerable lymphocytosis and eosinophilia. This similarity, despite the great difference in radiological findings between the advanced case of the father and the 4 mild cases, leads to the conclusion that the disturbance in blood formation is not merely the result of the displacement of marrow by new bone, but that there may be some central error responsible both for the abnormal ossification and the faulty haematopoiesis.

The history of this family confirms the theory of Westphal that the mild form of the disease, that is, the form from which this family suffers, is transmitted as a Mendelian dominant character, and that in this form the prognosis is relatively good. *Marianna Clark*

2554. **Heberden's Nodes. The Nature of Osteo-arthritis of the Fingers.** (Nodulos de Heberden. Naturaleza de la ósteoartritis de los dedos)

R. M. STECHER. *Revista Española de Reumatismo* [*Rev. esp. Reum.*] **3**, 310–323, Jan., 1950. 5 figs., 17 refs.

[This study is from Western Reserve University, not from Spanish sources.] It is interesting to learn that Heberden's original article, published in 1802, was less than 100 words long. Heberden's nodes nearly always affect the terminal phalanges, and the terminal joint may be pathologically flexed or laterally deviated. In young people the nodes are frequently traumatic in origin and they are painful, whereas in older patients, usually women at the menopause, they are painless. The frequency of the latter type increases with age. There is a definite familial incidence, more so on the maternal side. The condition is probably recessive so far as the father is concerned. As would be expected, a high proportion of the patients have osteo-arthritic changes in other joints—changes which are not usually incapacitating but are certainly symptomatic. There is no relation between Heberden's nodes and hypertension. For these nodes to develop it is essential for the nerve supply, both sensory and motor, to be intact. For instance, it was found that in a hemiplegic patient the nodes decreased in size on the affected side.

It is quite likely that the development of the nodes and of other osteo-arthritic changes is associated with a decreased blood supply. Cases of osteoporosis in relation to vasodilatation are rarely associated with Heberden's nodes. There is sometimes a disparity between radiological and physical signs. Lateral views frequently show greater osteophytic formation than do antero-posterior ones. Sometimes the proximal phalanges show osteo-arthritic changes, and there may be cyst formation in the terminal phalanges.

Treatment is useless, primarily because of the genetic factor. The author recommends that the patient be told that the condition is a benign form of osteo-arthritis which will not precipitate invalidism and must just be endured. *Paul B. Woolley*

Neurology

2555. **Positive and Negative Aspects of Hypothalamic Disorders**
B. BROUWER. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **13**, 16–23, Feb., 1950. 8 figs., 32 refs.

The author carried out clinical and histopathological studies in 15 cases of chronic hypothalamic disease, and embodies his findings in a discussion on clinical and experimental hypothalamic syndromes.

Diabetes insipidus, glycosuria, disorders of fat metabolism and genital function, defects in sphincter control, hyperthermia, visual disturbance, anomalies of sleep, growth disorders, and mental disturbances are discussed at varying length in relation to his case material and to quoted experimental effects of stimulation or injury of nuclear groups in the hypothalamus. Sometimes the clinical and experimental findings were in accord, but at other times he found it impossible to correlate them.

The clinical effects of hypothalamic lesions depend on the site and extent of the process, on its nature and speed of development, and on the age of the patient. Correlation of a particular syndrome with damage in a certain area can never be as exact clinically as experimentally; the one is a chronic and uncontrolled process, the other acute and more precise. Also a chronic lesion frequently allows development of compensatory mechanisms (for instance, the vegetative functions of certain cortical areas), and hypothalamic lesions may be found although symptoms had not been present during life.

To summarize, clinical syndromes may develop with hypothalamic disturbance corresponding to accepted experimental evidence; syndromes may occur and yet no lesion can be found post mortem; and lesions may be present in cases that had been symptomless during life.

[This paper provides a broad review, with an approach that is mainly clinical. Its value lies in this and not in the discussion of any particular syndrome.] *D. P. Jones*

2556. **The Longevity of Patients with Glioblastoma Multiforme**
M. G. NETSKY, B. AUGUST, and W. FOWLER. *Journal of Neurosurgery* [*J. Neurosurg.*] **7**, 261–269, May, 1950. 5 figs., 3 refs.

In a series of 70 cases of glioblastoma multiforme the average time between the appearance of the first symptom and death was 17 months. There were, however, 5 patients who survived for 6 years or longer and in this paper 2 of these cases are described. In the first, an operation was performed in October, 1933, and the tumour was verified histologically as glioblastoma multiforme. In the following years two courses of deep *x*-ray therapy were given. The patient died in July, 1943. At necropsy a left-hemisphere tumour was found which, on microscopical examination, was again proved to be glioblastoma multiforme.

The second patient was operated upon in February, 1939, when a cerebellar and brain-stem neoplasm was discovered; biopsy was performed and a diagnosis of astrocytoma was made. A course of deep *x*-ray treatment was given following the operation. The patient died in July, 1945. At necropsy a right cerebellar tumour was seen and was proved to be a glioblastoma multiforme. The corpus callosum was enlarged and contained numerous cysts which, on microscopical examination, were found to be astrocytic. *G. F. Rowbotham*

2557. **Therapeutic Studies on the Effects of Nervous Lesions on the Blood Pressure.** (Recherches thérapeutiques sur les accidents tensionnels provoqués par les lésions nerveuses)
G. TARDIEU, C. TARDIEU, J. SILVESTRE, and J. J. POCIDALO. *Revue Neurologique* [*Rev. neurol.*] **82**, 81–99, Feb., 1950. 17 figs., 1 ref.

This paper summarizes work by the authors and associates over a period of 8 years, in which 350 dogs were used. To imitate clinical lesions of the brain-stem, necrosing solutions were injected into the medulla. A few ml. of 30% alcohol produced the most marked effects, which may be grouped under three heads. (1) Breathing immediately stopped, and respiration had to be continued artificially. (2) Flooding of the air-passages might occur either from pulmonary oedema or from bronchial hypersecretion, but could easily be prevented by intravenous administration of morphine, *p*-aminobenzoic acid, " phenergan " (promethazine), or " dibenamine ". (3) The arterial blood pressure would rise briefly to 250 or 300 mm. Hg and then fall to 30 mm. in less than 30 minutes. Death invariably followed within 1½ hours. As the respiratory effects can be readily treated the authors concentrated solely on the treatment of the changes in blood pressure, using the time of survival as a measure of effectiveness.

The main principle of therapy is that drugs should be given by continuous infusion in adequate pharmacological doses. The authors consider that most other workers used doses too small to be effective; they themselves take the heroic view that if the necessary dose causes cessation of respiration, artificial respiration should be used and that this accident should be risked in preference to reducing the dose to below the " toxic " level.

Results and conclusions are as follows: (1) Drugs causing arteriolar constriction (yohimbine) accelerate death. This is assumed to be due to anoxic effect on the capillaries increasing the state of shock. (2) Drugs with an action on the capillaries have a palliative effect. Posterior pituitary hormone in doses up to 4 units per kg. per hour increased the survival rate, but left the blood pressure at about 30 mm. Hg. Doses up to 50 units per kg. per hour raised the pressure to 80 mm. Hg, but artificial respiration was required. The effect was very

variable. Two other drugs, " 3720 RP " and " 3885 RP " [formulae or chemical names not given], had a similar effect.

(3) Drugs with local analgesic action. Procaine in doses up to 250 mg. per kg. per hour was given without lethal effect provided artificial respiration was applied, indicating that its toxic effect is only on the respiratory centre. In spite of huge doses, some animals died in 3 hours; others survived, but the therapeutic effect could not be foreseen.

(4) Drugs blocking synaptic transmission. Nicotine in doses up to 10 mg. per kg. was without beneficial effect. Tetraethylammonium (TEA) in doses up to 600 mg. per kg. per hour (with artificial respiration) maintained the blood pressure of most animals above 100 mm. Hg for periods up to 5 hours. All animals eventually died, however, and it is notable that in spite of these doses the initial hypertension was rarely affected. The synthetic drugs " 3697 RP " (which has a curare-like action) and " 2987 RP " (" diparcol ", or diethazine hydrochloride) produced encouraging effects. The combination of TEA and D-tubocurarine was not especially effective.

Atropine accelerated collapse and death. The antihistaminic drugs mepyramine and promethazine were without effect, and the simultaneous use of TEA, atropine, and phenergan, although curative for shock after splanchnic irritation, had no effect in these cases.

The main conclusion drawn is that the circulatory shock following brain-stem damage involves reflex arcs, and that intensive therapy with drugs that hinder synaptic transmission gives the most encouraging results. Tetraethylammonium salts were the best of those tested, but it is hoped that better compounds will be found.

Donald McDonald

2558. **Spontaneous Thrombosis of the Carotid Arteries in the Neck. Report of Four Cases**

J. E. WEBSTER, S. DOLGOFF, and E. S. GURDJIAN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **63**, 942–953, June, 1950. 7 figs., 14 refs.

The authors call attention to the fact that the neurological abnormalities constituting a " stroke " may sometimes be the result of occlusion of the carotid arteries in the neck, and describe 4 such cases of their own with a review of previously reported cases from the literature. They find that spontaneous thrombosis of the carotid vessels in the neck may appear in four clinical forms: (1) the explosive form, simulating the usual cerebral vascular accident; (2) the slowly progressive form, with neurological symptoms of varying severity; (3) the form associated with visual disturbance and homolateral optic atrophy; (4) a silent form. Of the authors' 4 cases, 3 were cases of spontaneous thrombosis, in continuity, of common, external, and internal carotid arteries, and the fourth was one of thrombosis of the internal carotid alone. In all 4 cases the arteries were exposed at operation and found to be solid, rubbery, and devoid of pulsation. Portions were removed, and microscopical examination showed that atherosclerosis was the important aetiological factor, atheromatous plaques being found at the bifurcation of the common carotid artery in the fourth case.

Diagnosis may be made by palpation of the neck and the temporal arteries, although, as in the authors' 4th case, confusion may be caused by the pulsation of the external carotid artery in cases in which only the internal carotid is thrombosed. The final proof of the diagnosis must depend on exposure of the vessels.

[This last statement of the authors needs to be stressed in connexion with the picture occasionally occurring during percutaneous carotid angiography, when spasm of the internal carotid artery simulates thrombosis, but repetition of the investigation in 2 or 3 days reveals normal patency of the vessel.] *J. B. Stanton*

2559. **Symptoms and Signs of Intracranial Aneurysms, including Arteriovenous Aneurysms of the Carotid.** (La sémiologie générale et neurologique des anévrysmes intracraniens, y compris l'anévrysme artério-veineux de la carotide)

C. J. KETELAER. *Acta Neurologica et Psychiatrica Belgica* [*Acta neurol. psychiat., belg.*] **50**, 217–273 and 279–304, May and June, 1950. 7 figs.

2560. **Ascending Hemiplegia with Chronic Evolution (Syndrome of Mills).** (Hemiplegia ascendente de evolução cronica (sindrome de Mills))

D. COUTO. *Jornal Brasileiro de Neurologia* [*J. brasil. Neurol.*] **1**, 355–362, July–Sept., 1949. 5 refs.

The author reports a case of ascending hemiplegia similar to that described by Mills (*J. Amer. med. Ass.*, 1906, **47**, 1638). Over a period of 11 years the patient, a woman of 42, steadily developed a progressive weakness of the whole of the left side of the body, the weakness starting in her feet and ascending gradually until at the time of examination there was some slight facial asymmetry and definite, but not severe, weakness and wasting of the arm and leg. There were slight vegetative changes (lower temperature on the left side), but no sensory changes at all. Reflexes were typical of a pure pyramidal lesion. There were no other findings of note either clinically or pathologically, and the only clue to causation was a history of injury (not very severe) to the left ankle at the age of 20. No vascular, toxic, or infective cause was demonstrable, and serological reactions of blood and cerebrospinal fluid were uniformly negative. The diagnosis of disseminated sclerosis was rejected on the grounds that, while it was a possible explanation, the plethora of unusual features made it most improbable; that of amyotrophic lateral sclerosis was rejected because of the course, the one-sidedness, the lack of fibrillation and bulbar symptoms, the slightness of the atrophy, and the electrical reactions of the muscles. The author suggests that the syndrome described by Mills may be but one variety of what he has called " ascending neuropathy of traumatic origin ". *A. M. M. Wilson*

2561. **Ophthalmoplegic Migraine**

J. S. PATRIKIOS. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **63**, 902–917, June, 1950. 23 refs.

Psychiatry

2562. **The Psychological and Educational Problems of Left-handedness.** (Zum psychologischen und pädagogischen Problem der Linkshändigkeit)
T. KOHLMANN. *Wiener Zeitschrift für Nervenheilkunde* [*Wien. Z. Nervenheilk.*] **3**, 89–100, 1950. 3 figs., 9 refs.

The motor skill of both hands was measured by 16 tests in 50 left-handed apprentices aged 15 or 16. This allowed exact establishment of the degree of left-handedness; three types of this state could be differentiated, namely, frank left-handedness (the left hand being more useful in almost all tasks); intermediate left-handedness (the left predominating, but greater skill being shown with the right in several tests); ambidexterity (no great difference between right and left, or a somewhat greater degree of skill with the right). Training to work with the right hand is possible only in the ambidextrous. Correlation calculations showed that the left-handed man working with the right hand performs small movements more easily than large ones. In training to use the right hand, tasks involving small movements will be learned sooner than those involving large ones. *W. Forster*

2563. **Metabolic Disturbances and Hypopigmentation in Phenyl-pyruvic Oligophrenia.** (Les troubles métaboliques et l'hypopigmentation dans les oligophrénies phényl-pyruviques)
J. DELAY and P. PICHOT. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 1962–1967, June 2, 1950. 6 figs., 7 refs.

A brief review is given of the three known inborn errors of phenylalanine metabolism, namely, alcaptonuria, tyrosinosis, and phenylpyruvicuria, and 3 cases of this last disorder, with mental deficiency, are described. The degree of phenylpyruvicuria depends directly on ingestion of phenylalanine. Exsanguination-transfusion had no effect on the metabolic disorder in the one case in which it was tried. Since evidence of disturbance of liver function was found in all 3 cases, the hypothesis is put forward that the cause of the condition is a deficiency in the liver of an enzyme responsible for the breakdown of phenylalanine into tyrosine, and of phenylpyruvic acid into 2 : 5-dihydrophenylpyruvic acid. The metabolic disorder is transmitted as a recessive character and appears to be linked with a character causing diminished pigmentation of the hair. *H. K. Goadby*

2564. **Psycho-infantilism.** [In English]
B. J. LINDBERG. *Acta Psychiatrica et Neurologica* [*Acta psychiat., Kbh.*] Suppl. 61, 1–126, 1950. 39 refs.

This monograph deals with psychiatric aspects of "psycho-infantilism". The author defines psycho-infantilism as "a persistence in the adult of mental qualities characteristic of the child". The most common traits are: helplessness, desire for guidance and protection, and excessive dependence associated with a strong emotional fixation on one of the parents. Basing his views on 30 cases described in detail, the author discusses the relation of emotional immaturity to various psychiatric disorders, and attempts to trace the aetiological factors responsible for psycho-infantilism. Most of the patients suffered from acute reactive depression, anxiety states, or obsessions with hysterical trends. Emotional immaturity leads to maladjustment and makes the individual more vulnerable to environmental stresses. The emotionally immature person is prone to break down when faced with an important decision, especially when deprived of the protection of the person on whom he relied. Psycho-infantilism is often seen in psychosomatic disorders, and according to some observers is quite common in patients with duodenal ulcer.

In discussing the relation of emotional immaturity to personality disorders, the author follows the views of Sjöbring. (A fuller account of Sjöbring's theories is given in English in *Acta psychiat., Kbh.*, Suppl. 16.) Emotional immaturity is often associated with some of the "minus variants" of the personality such as subvalidity (psychoasthenic-obsessional attitudes), substability (syntonic attitudes), subsolidity (hysterical attitudes), and subcapacity (intellectual inferiority). Schizoid features are almost entirely absent.

In the formation of psycho-infantile traits, adverse environmental factors during childhood play the most prominent part. In 24 of the 30 reported cases the patient was brought up under circumstances which hindered the normal process of "psychological weaning". Physical inferiority was found to be of no importance as such, but it often led to the occurrence of unhealthy psychological situations (domineering and over-protective parental attitudes). Emotional immaturity often prevented the individual from accepting the responsibility of marriage and setting up a family. Impotence, frigidity, or sexual promiscuity were not uncommon, whereas in other cases the childish striving for unrestricted pleasure could be traced in excessive drinking. In conclusion the author insists that psycho-infantilism is not a disease; it is often associated with personality disorders and is responsible for many minor psychotic reactions. *J. T. Leyberg*

2565. **The Dinitriles in Psychiatric Therapy.** (Os dinitrilos na terapeutica psiquiatrica)
D. FURTADO. *Actas Luso-Españoles de Neurología y Psiquiatría* [*Act. luso-esp. Neurol. Psiquiat.*] **9**, 83–96, May, 1950. 12 refs.

Because nitriles have been shown to increase the amount of proteins and nucleotides in nerve cells, and because specimens taken at leucotomy show an abnormally small amount of these substances in nerve cells, it has been suggested that schizophrenia should be

treated with these drugs. Favourable reports of such treatment have been given by Swedish and French authors.

The present author treated 8 cases of melancholia in the City Hospital, Lisbon, by intravenous injections of malonyl and succinyl nitrile. The results were disappointing, for only in 2 cases was slight improvement noted. *S. S. B. Gilder*

2566. **A Test which Predicts the Clinical Effects of Electric Shock Treatment on Schizophrenic Patients**
D. H. Funkenstein, M. Greenblatt, and H. C. Solomon. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **106**, 889–901, June, 1950. 19 figs., 4 refs.

The authors, working at the Department of Psychiatry, Harvard Medical School and at the Boston Psychopathic Hospital, have evolved a test by which they believe they can predict the clinical response, in cases of schizophrenia, to electric convulsion therapy (E.C.T.). The autonomic responses to certain drugs, before and after E.C.T., in 48 cases of schizophrenia were compared with those in 21 cases of manic-depressive psychosis, 12 of psychoneurosis, 13 of involutional psychosis, and 6 of miscellaneous conditions. On the first day of the test the patient was given 1 ml. of normal saline intravenously, on the second day 0·05 mg. of adrenaline hydrochloride in 0·5 ml. of water intravenously, and on the third and final day 10 mg. of "mecholyl" (methacholine hydrochloride) intramuscularly. After the injections of normal saline and adrenaline the systolic blood pressure was noted at intervals until it returned to its initial level; after the injection of mecholyl it was noted for 25 minutes. Notes of other autonomic phenomena and of the effect on anxiety were also made. The tests were carried out within 3 days of the first electric shock and repeated 2 to 5 days after the last shock. The authors distinguished, largely on descriptive grounds, seven different patterns of blood-pressure response and four types of psychophysiological response to the two drugs. While these patterns were not specific for any condition, the majority of cases in each diagnostic category tended to fall within the same group, except for the schizophrenics, who were distributed amongst all groups. However, the small number of schizophrenics who fell within the groups which were generally associated with the affective psychoses were found to respond to E.C.T. In other words, when the schizophrenic patient's pattern of autonomic response corresponded to that of the majority of affective psychotics, he responded to E.C.T.

After treatment it was found that in 41 of the 89 cases the pattern of response had altered. Irrespective of diagnosis, those patients whose symptoms of anxiety became worse after injection of adrenaline were usually worsened by E.C.T., whereas those who responded with a rigor or an exacerbation or relief of anxiety after injection of mecholyl responded dramatically to E.C.T.

[Nine short case histories are given. Reference is made to controls but these are not described. The delimitation of the patterns of response is impressionistic and is based on small numbers.] *Hunter Gillies*

2567. **Antabus and the Metabolism of Alcohol**
H. W. Newman. *California Medicine* [*Calif. Med.*] **73**, 137–140, Aug., 1950. 11 refs.

The author studied the metabolism of alcohol and acetaldehyde before and after the administration of "antabus" (tetraethylthiuram disulphide) in a series of experiments carried out at Stanford University, San Francisco. In 2 dogs under pentobarbitone anaesthesia the decrease in blood alcohol concentration during a period of 6 hours after the intravenous injection of 1 g. of alcohol per kg. body weight was 12·2 mg. and 14·4 mg. per 100 ml. respectively, alcohol still being present in the blood at the end of the period. At the same time the blood acetaldehyde content rose slowly to final levels of 0·2 mg. and 0·3 mg. per 100 ml. respectively. These findings are in accordance with those of other workers, the acetaldehyde presumably being derived from the breakdown of alcohol and being itself broken down almost as rapidly as it is formed. However, when acetaldehyde was infused intravenously at a rate of 185 mg. per kg. per hour, equivalent to the maximum rate of its formation from alcohol, there was an initial rapid rise in blood acetaldehyde level to about 1·5 mg. per 100 ml., followed by a fall to levels similar to those found after the infusion of alcohol; a similar, though less marked, initial rise occurred when the infusion was repeated at a rate of 100 mg. per kg. per hour. This apparent delay in initiation of the process of acetaldehyde breakdown has not previously been reported and the reason for it is obscure.

The above experiments were then repeated on the same animals after a week's treatment with antabus, 0·125 g. daily. The rate of disappearance of alcohol from the blood was not significantly affected by the previous administration of antabus, but the blood acetaldehyde level rose to about 0·6 mg. per 100 ml. immediately after the injection of alcohol; however, it subsequently fell and at the end of 6 hours was actually lower than when no antabus had been given. A similar result was obtained when acetaldehyde was infused at the rate of 100 mg. per kg. per hour, indicating that the effect of antabus on acetaldehyde metabolism was independent of the source of acetaldehyde. On the other hand, infusion of acetaldehyde at the rate of 185 mg. per kg. per hour resulted in a progressive rise in blood acetaldehyde level in the 2 dogs to 2·0 mg. and 4·0 mg. per 100 ml. respectively after 6 hours.

While these experiments confirm that the effect of antabus is not to accelerate production of acetaldehyde from alcohol, but to delay its further breakdown, that effect appears to be more marked at the beginning of the period of its production (or infusion), the reason for which is obscure. That the inhibitory effect of antabus is not confined entirely to the initial stages is indicated by the results of the last experiment, but the author points out that even here it is not so great as might appear, the average blood acetaldehyde level after 6 hours being barely 3% of that to be expected if its breakdown were completely prevented. *D. I. Crowther*

See also Sections Medical Jurisprudence, Abstract 2306; Paediatrics, Abstract 2412.

Infectious Diseases

VIRUS INFECTIONS

2568. **Mumps Orchitis and Testicular Atrophy. I. Occurrence. II. A Factor in Male Sterility**
C. A. WERNER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **32**, 1066–1086, June, 1950. 7 figs., bibliography.

The occurrence of orchitis after mumps has been known since the time of Hippocrates, and everyone is familiar with the danger of post-orchitic atrophy due to direct action of the virus on the seminiferous tubules and to the pressure of exudate and oedema upon the tubules within a taut tunica albuginea. Although it has long been generally believed that orchitis following mumps may play a part in causing male sterility, little evidence on this point has been published and the belief has been called a " myth " by French authors. Reported estimates of the frequency of impairment of fertility due to post-orchitic atrophy vary from *nil* to 4%. Of 2,000 patients examined by the author in a military camp, 1,086 knew they had had mumps in the past; 53 of these (4·9%) had had orchitis as a complication, and 19 of them had some form of testicular atrophy, which was usually symptomless and unilateral.

In another investigation a group of 49 men with a clear history of post-orchitic atrophy were examined as to the quantity and quality of semen, and very elaborate biochemical tests were made upon the product of the tubules. In 50% the semen was found to be subnormal. But a similar test upon 91 presumably normal and healthy men of a similar age group revealed that in 38% of these the semen was also subnormal. Elaborate statistics are presented from which it is concluded that of all post-adolescent males who contract mumps, 1·7% develop severe orchitis leading to considerable atrophy, and of these 13% have impaired fertility.

G. F. Walker

2569. **Guillain–Barré Syndrome and Acute Hepatitis.** (Sindrome de Guillain–Barré e hepatite aguda)
J. V. COLARES, C. MONTEIRO, and J. R. DA SILVA. *Jornal Brasileiro de Neurologia* [*J. brasil. Neurol.*] **1**, 385–391, July–Sept., 1950. 8 refs.

Interest in the Guillain–Barré syndrome is mainly centred on its aetiology. French and North American authors favour infection, especially by a virus, as the cause: Guillain and Barré suggested that it might be toxic or infective. Pette in Germany believes it to be an allergic manifestation, and points out that in polyneuritis due to deficiencies or toxins there are no changes in the cerebrospinal fluid (C.S.F.), while in those due to infection there is usually a pleocytosis. The high protein content with relatively few cells corresponds with the situation in the exudate in " serous inflammation " described by Rössle and Eppinger and thought by them to underlie many allergic phenomena. There may well be a variety of causes, however, and the syndrome is known to follow influenza, diphtheria, pneumonia, and the exanthemata.

The authors report a case of the Guillain–Barré syndrome in a man of 43 with polyneuritis, homologous serum jaundice, and eosinophilia. He received several transfusions after subtotal gastrectomy for chronic duodenal ulcer and 10 weeks later developed jaundice, pains and paraesthesiae in all four limbs, and weakness of his legs. A week later he had a flaccid paralysis of his legs with loss of knee-jerks and ankle-jerks, and a right facial palsy (of lower motor neurone type) and diplopia due to an external rectus palsy. The C.S.F. contained 16 leucocytes and some erythrocytes per c.mm., and the protein content was 500 mg. per 100 ml. Nonne and Pandy reactions were positive and the fluid was sterile. The Takata-Ara reaction was positive in both blood and C.S.F. The liver was enlarged and liver function tests confirmed the presence of hepatocellular damage. Except for an eosinophilia of 28% the blood picture was normal. Recovery was uneventful and apparently complete both clinically and chemically.

The association of the Guillain–Barré syndrome with acute hepatitis is very rare. The authors think that the very high protein level and few cells in the C.S.F., coupled with eosinophilia, represent an allergic response to infection similar to that suggested by Iversen (*Acta med. scand.*, 1948, **129**, 441), though realizing that the " serous inflammation " of Rössle and Eppinger is part of the picture of acute hepatitis.

A. M. M. Wilson

See also Section Microbiology, Abstract 2394.

2570. **Clinico-pathological Features of Neuroviral Infections Observed in Brazil.** (Algumas considerações clinico-patológicas acerca das neuroviroses observadas no Brasil)
A. AUSTREGESILO, D. COUTO, —. AUSTREGESILO, and N. COSTA. *Jornal Brasileiro de Neurologia* [*J. brasil. Neurol.*] **1**, 363–375, July–Sept., 1950. 14 figs.

The authors give a general survey of the virus diseases of the nervous system occurring in Brazil.

Cases of encephalitis and encephalomyelitis were first recorded in Brazil in the 1918 influenza epidemic, when hypersomnia and ocular palsies occurred but hyperkinetic states were rare. Since then both spinal and cerebral types of case have increased, as in the rest of the world. The widely accepted relationship of this increase to more rapid and frequent travel by man is demonstrated by the occurrence of local outbreaks near airports.

Localization of the virus in the brain is usually shown by apathy or torpor; there is leucocytosis in the blood, and the cell and protein content of the cerebrospinal fluid (C.S.F.) is raised. Children in these conditions are nearly always febrile, adults often are not.

Austregesilo observed in 1937 a peculiar form of neuromyelitis. There was a first stage with symptoms of a general infection and sensory changes (paraesthesiae and pain, especially in the legs) and weakness which sometimes progressed to paralysis. There was hypotonia and depression of the reflexes, and an increase in cells and protein in the C.S.F. This stage, suggestive of polyneuritis, was often transient and the illness was usually regarded as influenza or some unrecognized infection. The second, much more serious, stage followed days, weeks, or months later with motor, sensory, sphincteric, and bulbar disturbances, often leading to death. Cases showing only some of these features were common, as in one group in which an isolated brachial palsy was the commonest finding. Neurotropic myelitis and types of encephalitis associated with children's diseases are rare in Brazil, benign lymphocytic meningitis less so, and the Guillain–Barré syndrome is common.

Chronic encephalitis is usually of the hypertonic, hyperkinetic type. Parkinsonism is increasing, but the commonest sequelae are disorders of mood and behaviour.

No new virus has been described, but a strain isolated from a case of encephalitis was maintained for two passages in animals and was agglutinated by the serum of the patient's dog. Some veterinary work has been done and antibodies to a mosquito-borne virus affecting rats were found in some of those working on the problem.

Histologically, fulminating infections show damage to the whole neuraxis and to the meninges as well, being really cases of myelo-encephalomeningitis. Clinically they correspond to Landry's paralysis. Chronic infections show a selective destruction of the substantia nigra. *A. M. M. Wilson*

2571. **Infection of Laboratory Workers with Coxsackie Viruses**

E. W. Shaw, J. L. Melnick, and E. C. Curnen. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 32–40, July, 1950. 2 figs., 7 refs.

The authors describe 6 cases of laboratory infection with three strains of Coxsackie virus. The virus was recovered from faeces or from throat swabs. The clinical features varied from those associated with epidemic pleurodynia to " non-paralytic poliomyelitis "; and in one patient whose cerebrospinal fluid was examined there was a pleocytosis. Neutralizing antibodies developed after infection: they were not present before infection. *G. M. Findlay*

POLIOMYELITIS

2572. **Poliomyelitis and Immunization against Whooping-cough and Diphtheria**

H. S. Banks and A. J. Beale. *British Medical Journal* [*Brit. med. J.*] **2**, 251–252, July 29, 1950. 4 refs.

The relation between immunizing injections and poliomyelitis is discussed with special reference to cases admitted to the Park Hospital, London, from 1947–9.

Of 111 patients with paralysis seen in this period 14, all children under the age of 5, had received one or more injections within the previous 2 months. In most cases the onset of paralysis occurred from 9 to 14 days after the injection. In 9 cases paralysis followed injection of combined pertussis and diphtheria prophylactic, in one case pertussis prophylactic alone, and in 4 cases diphtheria prophylactic only. The paralysis, which affected much the same group of muscles in all cases, was not associated with any particular technique or locality. The authors conclude that during periods of high prevalence of poliomyelitis there is a definite, though small, risk that serious limb paralysis, affecting mainly muscles adjoining the site of injection, will follow inoculation with the types of pertussis and diphtheria prophylactic commonly used in Britain. They do not advance any theory to account for this remarkable phenomenon. *Jos. B. Ellison*

2573. **Evolution of Neurologic Signs of Early Anterior Poliomyelitis**

L. J. Pollock, B. Boshes, I. Finkelman, F. Hiller, H. Chor, M. Brown, A. J. Arieff, E. Liebert, E. L. Tigay, M. Schiller, and I. C. Sherman. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **79**, 973–987, June, 1950. 9 figs., 11 refs.

Thinking that frequent and detailed observation of single cases of paralytic poliomyelitis might reveal more of the natural history of the disease than does the analysis of large numbers of cases less frequently examined, the authors studied 30 such cases at frequent intervals by day and night at a hospital for infectious diseases. Observations upon an additional 12 cases, with meningeal symptoms only, are included. The following are the more important findings:

No muscle spasm was encountered while paralysis was developing; tenderness and stretch pain were found infrequently and only where paralysis had occurred. Of the signs indicative of " meningism ", namely, neck rigidity and the Kernig, Brudzinski, and Lasègue signs, it was observed that, in contrast to cases of meningitis proper, the characteristic positive responses were often not obtained until a fairly wide movement of the test area had been made. Moreover in poliomyelitis the Kernig and Lasègue signs tended to appear late. In most of the paralysed cases the peak of paralysis was reached between the 75th and 150th hours after the first symptom or sign of disease. Variation in the extent of paralysis of affected muscles from hour to hour was noteworthy. In one-fifth of paralysed muscles a period of improvement was followed by more profound paralysis.

The deep reflexes were also variable from hour to hour in the same patient; in general, however, the earlier that deep reflexes disappeared the more likely was it that muscle groups involved would become paralysed. The abdominal reflexes were often hyperactive when no paralysis, or paralysis of the upper extremities only, was destined to develop, whereas abolition of these reflexes was usual if severe paralysis of the lower limbs was to ensue. An extensor plantar reflex was found fleetingly in several instances. There was no correlation between this sign and absence of abdominal reflexes or hyperactive

deep reflexes, although the latter findings were not uncommon by themselves. Lesions of the upper motor neurone are therefore considered uncommon in this disease.

Myotatic irritability was often increased in paralysed muscles, more especially of the upper limbs. This also showed great fluctuation in severity from hour to hour in the same case. *M. MacGregor*

2574. **Observations on the Use of Aureomycin in the Treatment of Acute Anterior Poliomyelitis**
E. Weis and B. J. Winston. *Illinois Medical Journal* [*Illinois med. J.*] **98**, 9–11, July, 1950. 4 refs.

Claims are made that a daily dose of 2 g. aureomycin is of value in poliomyelitis. Of 16 patients who received 2 g. aureomycin or more a day 14 recovered completely and 2 had residual paralysis. Of 32 patients who received less than 2 g. per day 24 recovered, 7 had residual paralysis, and 2 with bulbar poliomyelitis died. Of 4 patients who received no aureomycin, including one case of bulbar involvement, none recovered. The average duration of fever in those receiving less than 2 g. daily was 4·4 days; in those given at least 2 g. daily 2·3 days. In the group given small doses of aureomycin there were 10 patients with paralysis, and 2 recovered; in the group given 2 g. or more daily there were 8 with paralysis and 6 of these recovered. It is considered that these differences are statistically significant and that further clinical trials are warranted. [No attempt was made to isolate a virus in these cases and the diagnosis depended on clinical findings and the evidence of pleocytosis in the cerebrospinal fluid. The authors themselves bring up the question whether some patients may not have been suffering from Coxsackie virus infection. In mice injected with the Lansing strain of poliomyelitis, aureomycin has no effect on the course of the infection.] *G. M. Findlay*

2575. **Poliomyelitis of the Newborn. Pathologic Changes in Two Cases**
J. L. Baskin, E. H. Soule, and S. D. Mills. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 10–21, July, 1950. 4 figs., 22 refs.

The authors review 10 cases of neonatal poliomyelitis in the literature and describe 2 of their own. The first baby was born while the mother was in a respirator with poliomyelitis. The baby was immediately isolated from the mother, but became febrile on the 3rd day after birth and on the 5th day developed a right-sided paresis and bulbar symptoms. The cerebrospinal-fluid (C.S.F.) changes were typical of poliomyelitis, and the child died on the 7th day. There were typical changes of polio-encephalitis in the cord, medulla, pons, mid-brain, cerebellum, thalamus, and the motor areas of the cortex, with notable degenerative changes in the grey matter of the anterior horns of the cervical and lumbar enlargements.

In the 2nd case, the mother developed signs of poliomyelitis 2 days after the birth of her chlid. Eight days after birth the baby became febrile, and on the 9th day a flaccid paresis developed. The C.S.F. was normal on the 5th day, but showed changes typical of poliomyelitis on the 11th day, the child dying on the 14th day after birth. Histologically, there was a severe myocarditis, with typical changes of poliomyelitis chiefly in the cord and medulla.

The authors point out that in the first case either the incubation period was 3½ days, which is less than the accepted minimum incubation period, or the infection was intrauterine in origin. *R. S. Illingworth*

2576. **Electrocardiographic Observations in Poliomyelitis. Changes of the Q–T Interval in Twenty-three Cases**
H. A. Joos and P. N. G. Yu. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 22–33, July, 1950. 3 figs., 35 refs.

The authors studied the electrocardiogram in 23 cases of poliomyelitis and 55 healthy children without evidence of cardiovascular disease. They measured the Q–Tc interval, calling 0·405 second the upper limit of normal, and any increase up to 5% "equivocal". They found prolongation of the Q–Tc interval in 5 cases of poliomyelitis and an equivocal change in 3. There was an equivocal change in 3 controls. *R. S. Illingworth*

2577. **The Excretion of Poliomyelitis Virus by Healthy Family Contacts.** (De uitscheiding van poliomyelitisvirus door gezonde contactpersonen)
J. D. Verlinde and E. Nihoul. *Nederlandsch Tijdschrift Voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **94**, 1186–1195, April 29, 1950. 18 refs.

A poliomyelitis virus, strain Rieth.A.K.1949, was isolated from the faeces of a 2-year-old patient and of healthy children of the same family. After cynomolgus-monkey passage the patient's virus was virulent for cynomolgus monkeys in a 10^{-3} dilution, whereas the virus recovered from the healthy contacts caused paralysis in monkeys only in a 10^{-1} dilution. In cross-immunity experiments, the virus appeared not to be related to the Lansing type, the Aycock strain, or to the Columbia SK virus. No antibodies against the Lansing type could be demonstrated in the patient's serum in the acute phase or in convalescence.
J. D. Verlinde (*Excerpta Medica*)

2578. **The Treatment of Pain and "Spasm" in Poliomyelitis with "Priscoline"**
W. O. Geisler, W. T. Mustard, and C. S. Anglin. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **63**, 60–63, July, 1950. 3 figs., 13 refs.

2579. **Priscoline for Pain in Poliomyelitis**
W. A. Reilly and A. H. Barsanti. *Journal of Pediatrics* [*J. Pediat.*] **36**, 711–714, June, 1950. 9 refs.

Many workers have suggested that the sympathetic nervous system is involved in acute poliomyelitis and, if this is so, it would be reasonable to assume that drugs with an adrenaline-like action would relieve spasm and thus diminish pain. "Priscoline" (2-benzyliminazoline hydrochloride) has such an action and its effect in 35 cases of poliomyelitis has been studied. The drug is given intramuscularly in an initial dose of 10 mg. for

children under 5 years, the dose being increased by 5 mg. every 4 hours until flushing occurs; correspondingly higher doses are given for older children. The assessment of the severity of pain is difficult, especially in young subjects, but the authors consider that 16 of the 35 patients derived no benefit from the drug, in 4 doubtful benefit followed its use, in 8 the pain was relieved, and in 8 the drug's action could not be assessed. Nausea, vomiting, pruritus, and paraesthesiae may occur as toxic manifestations, and hypertension followed its administration in 7 cases. Because of the fluctuating blood pressure in bulbar poliomyelitis priscoline is contraindicated. Hot packs are superior to the drug in the relief of pain and spasm in most cases. *R. M. Todd*

2580. **Serum Potassium in Poliomyelitis**
A. M. EARLE. *Journal of Pediatrics* [*J. Pediat.*] **36**, 715–720, June, 1950. 21 refs.

Low serum potassium levels have been demonstrated in familial periodic paralysis and in other conditions causing paralysis. The relation between serum potassium level and severity of paralysis in poliomyelitis was investigated in 56 patients, and the results in 32 of them are described in detail in this paper. In the majority of patients on admission the paralysis was severe and no other condition which might affect potassium balance was present. In 9 patients the serum potassium level was normal and on discharge there was no residual paralysis. In 9 others the serum potassium level was normal and on discharge there was residual paralysis or weakness of isolated muscle groups. In 14 cases, 4 with severe bulbar involvement, low serum potassium values were obtained, but no clinical improvement followed the oral administration of potassium, although the serum potassium level returned to normal. *R. M. Todd*

RICKETTSIAL INFECTIONS

2581 (*a*). **A Case of Brill's Disease in London**
J. C. HAWKSLEY and E. J. STOKES. *Lancet* [*Lancet*] **2**, 97–99, July 15, 1950. 1 fig., 19 refs.

Brill's clinical suspicion that a febrile disease which he observed among the immigrant population of New York between 1896 and 1910 was a mild endemic form of louse-borne typhus fever was confirmed by the experimental work of Anderson and Goldberger (1912), Mooser (1929), and Zinsser and Castaneda (1933), Zinsser's conclusion that cases observed in the north-western United States in 1934 were due to a recrudescence of old infections originally acquired in European foci was confirmed serologically by Plotz, who found the same complement-fixation reactions in New York cases as are found in cases of louse-borne typhus in Europe. Evidently *Rickettsia prowazeki*, the causative agent of louse-borne typhus, persists indefinitely in some patients after recovery and, when their resistance is subsequently lowered, may induce a mild attack of the disease. (Incidentally, the endemic typhus of the south and south-eastern United States, which until 1929 was also regarded as " Brill's disease ", was eventually proved to be murine typhus, identical with Mexican typhus and now known to have a world-wide distribution.)

The present authors describe the case of a woman aged 49 who developed a febrile illness, with headache and pains in the limbs, which was treated with sulphadimidine (" sulphamezathine ") without effect. The symptoms had not changed by the 8th day of illness, when the patient was admitted to hospital. The temperature was then 102° F. (38·9° C.) and there was suffusion of the conjunctivae, but no rash was present and the spleen was not palpable. Her temperature began to fall after admission to hospital and was normal after 8 days. The patient was born in Poland and had typhus there in 1915; she migrated to Berlin in 1919, and to London in 1939. A tentative diagnosis of Brill's disease was made and investigations (blood count, blood culture, faeces culture, and agglutination tests) were undertaken. All were negative except the Weil–Felix tests, in which an agglutination titre of 1 in 700 to *Proteus* OX19 antigens was obtained on the 16th day of illness, subsequently falling rapidly. Samples of serum were sent for further investigation to Felix, whose opinion was that the marked fall in the OX19 titre was to be accepted as confirming the clinical diagnosis (see Abstract 2581 (*b*)). Specimens of serum were also sent to Washington for rickettsial agglutination and complement-fixation tests, the reactions being reported as " definitely epidemic in type and . . . consistent with a diagnosis of Brill's disease ". *J. V. Armstrong*

2581 (*b*). **A Note on a Case of Brill's Disease in London**
A. FELIX. *Lancet* [*Lancet*] **2**, 99–100, July 15, 1950. 15 refs.

Apart from one case reported by Mooser and Loeffler in 1946 in Zurich, all the reported cases of Brill's disease have occurred in the coastal towns of the north-eastern United States. Although the majority of cases have been in Jewish immigrants from eastern Europe, the incidence is not limited to any racial group. It seems likely that the disease will occasionally be seen in any country whose population includes an appreciable proportion of persons previously exposed to louse-borne typhus.

The clinical diagnosis of Brill's disease is not easy, as the disease is always sporadic and the clinical course milder than in the primary attack of louse-borne typhus. In the present case (see Abstract 2581 (*a*)), the patient did not even develop a rash, which is the most helpful of the few diagnostic signs. Laboratory tests are indispensable for diagnosis and, although agglutination and complement-fixation tests became available recently and are valuable in differentiating the varieties of typhus, the case under review shows clearly that it was possible to confirm the diagnosis by the use of the *Proteus* OX19 reaction; incidentally, it became positive at an earlier stage than the rickettsial agglutination reaction.

It is important, however, that the Weil–Felix test be standardized by international agreement. The customary use of Dreyer's technique is unsatisfactory because of the heat-lability of O agglutinins. The proper technique entails the use of round-bottomed tubes and incubation at 37° C. (Felix, *Trans. R. Soc. trop. Med. Hyg.*, 1944,

37, 321). How great is the need for standardization is shown by results published by Murray *et al.* (*J. Amer. med. Ass.*, 1950, **142**, 1059), who noted that only 3 out of 14 sera from patients with Brill's disease gave a diagnostic agglutination titre in the Weil–Felix test. The indications are that the technique employed was unsatisfactory, dilutions as low as 1 in 10 being used. In the London case the tests carried out in two laboratories showed a fourfold difference in titre.

From the epidemiological point of view Brill's disease is of interest as a possible source of dissemination of louse-borne typhus, and in view of the widespread epidemics of this form of typhus during the last war and the subsequent movement of large groups of people from one country to another, the disease may come into prominence in many parts of the world.

J. V. Armstrong

2582. **Does Typhus Produce Life-long Immunity?** (Hinterlässt des Fleckfieber eine lebenslängliche Immunität?)
F. V. BORMANN. *Deutsche Medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **75**, 826, June 16, 1950.

Many case reports from all over the world have shown that typhus does not confer permanent immunity and that re-infection occurs frequently, even a relatively short time after the primary disease. The second illness may be more severe than the first attack, though as a rule it is milder. One observer has reported 13 attacks of typhus in one patient.

For this report, 259 inhabitants of a village where typhus is endemic were observed during a recent outbreak. All the 259 had had typhus once in their life, 74 before 1918, 108 during 1918 to 1922, and 77 during 1933 to 1934. In the outbreak of 1941–3, 66 inhabitants contracted the disease (25·5%). Diagnosis was confirmed by agglutination reactions. The 66 persons were spread throughout the three groups; 55 had a typical attack and 15 of these were seriously ill, but none died. Eleven of the 66 had abortive, but serologically proved, attacks.

The author concludes that an attack of typhus confers a lengthy and fairly reliable, but not a permanent, immunity. Second attacks are mostly mild and hardly ever fatal.

W. Stern

BACTERIAL INFECTIONS

2583. **Tolerance to the Action of Endotoxins of Enteric Bacilli in Patients Convalescent from Typhoid and Paratyphoid Fevers**
F. A. NEVA and H. R. MORGAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **35**, 911–922, June, 1950. 12 refs.

It has already been shown that tolerance develops in man and animals to the pyrogenic effect of the endotoxins, or somatic antigens, of the enteric organisms after repeated injections. In the present work, this is shown to hold for persons recovering from enteric fever. The endotoxins were given intravenously on 4 successive days, the doses being 5 μg.typhoid antigen, 1 μg. shigella antigen, 25 μg. typhoid antigen, and 5 μg. shigella antigen successively. This course of injections was followed by a marked febrile response in 16 out of 17 healthy control subjects; 12 were given a second course 17 weeks later and showed considerable tolerance to the pyrogenic effect. The tests were repeated on 22 patients recovering from typhoid fever; the febrile response was considerably less than that seen in the controls; similar results were obtained in 14 patients recovering from paratyphoid-A infection. No correlation was observed between the magnitude of the febrile response and the titre of serum antibodies. No tolerance to the pyrogenic effect, or only a slight degree of tolerance, was seen in 12 patients recovering from bacillary dysentery, salmonella enteritis, and other miscellaneous infections.

D. J. Bauer

2584. **The Treatment of 100 Cases of Typhoid Fever with Chloramphenicol ("Chloromycetin"). I. Clinical Aspects. II. New Biological Problems. III. Therapeutic Technique.** (Les aspects cliniques de la fièvre typhoïde traitée par la chloromycétine. Les problèmes biologiques nouveaux de la fièvre typhoïde traitée par la chloromycétine. La conduite thérapeutique dans la fièvre typhoïde traitée par la chloromycétine)
E. BENHAMOU, F. DESTAING, E. ALBOU, G. DALEY, P. GRIGUER, and A. SORREL. *Semaine des Hôpitaux* [*Sem. Hôp. Paris*] **26**, 219–229, 230–232, and 232–235, Jan. 22, 1950. 18 figs., 31 refs.

Cases treated with chloramphenicol consisted of 56 cases of typhoid fever and 6 of paratyphoid (A, B, and C) infection, together with 8 cases of relapse, 7 associated with complications, and 23 of an encephalitic type. In true typhoid fever there was a quick fall in temperature, usually within 4 days. The rapidity with which the patient became afebrile depended on the duration of the fever before treatment. The total dose given was usually between 22 and 40 g. In paratyphoid fever the fall in temperature was not so rapid, usually taking place over 6 to 10 days. Relapses were characterized by the frequency (2 or 3 times) with which they recurred, within 10 to 25 days after an apparent clinical cure. These benign relapses could be prevented by giving more prolonged treatment over a period of about 2 weeks. The complication rate was lowered by chloramphenicol therapy, but intestinal haemorrhage and perforation (4 cases) and myocarditis (3 cases) were observed. The encephalitic cases, with tremors and myoclonus, were the least influenced by the drug. Of 23 patients, 12 were cured and 11 died. There were, however, 86 cures out of the 100 cases treated, details of which are given.

The micro-organisms isolated in these cases included 37 strains of *Salmonella typhi*, 3 strains of *S. paratyphi* A, 1 strain of *S. paratyphi* B and 1 strain of *S. cholerae suis*. When treatment was given early, blood culture rapidly became negative, but when treatment was delayed, culture remained positive for a long time. The sensitivity of the strains was tested *in vitro* against chloramphenicol, aureomycin, and streptomycin. The minimum effective amounts of these substances were 3·1 to 6·2 μg. for

chloramphenicol, 0·8 to 25 μg. for aureomycin, and 15·5 to 134 μg. for streptomycin per ml. of medium. Chloramphenicol was the most effective and no decrease in sensitivity was encountered. Electrophoresis experiments showed a considerable rise in gamma-globulin level in the blood in encephalitic cases.

The authors recommend that treatment with chloramphenicol in typhoid fever should begin as early as possible with an initial loading dose of 4 g., followed by 3 g. daily until the fever has abated, 2 g. being then given daily (in divided doses every 4 hours) for a total period of at least 2 weeks. By prolonged administration, it is stated, relapses are prevented. In serious cases the concurrent use of aureomycin is advised. Gastric symptoms were the most frequent side-effects observed. Stomatitis, cheilitis, and sometimes pharyngitis appeared very soon and the patients complained of dysphagia and burning gastric pains. Examination revealed a pink dry tongue and a red, oedematous pharynx. Vomiting was frequent, particularly in children, even with moderate doses. Chloramphenicol, however, remains the drug of choice in the treatment of typhoid fever. There were 86 cures out of 100 cases treated and, excluding the encephalitic types, there were 76 cures out of 78 cases of typhoid infection. *R. Wien*

See also Section Pharmacology and Therapeutics, Abstract 2272; and Section Microbiology, Abstract 2400.

2585. **Fatalities in Salmonella Infections**
I. SAPHRA. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 74–77, July, 1950. 6 refs.

During a period of 10 years ending in April, 1949, nearly 5,000 salmonella cultures were identified at the New York Salmonella Center. An examination of the records in the 3,279 cases of human infection revealed that 174 fatalities occurred, 26 salmonella types being isolated from these fatal cases. The most virulent types were *Salmonella typhi-murium*, *S. cholerae suis*, *S. oranienburg*, and *S. newport*. The infection was with *S. typhi-murium* in 63 of the fatal cases and with *S. cholerae suis* in 40. The fatality rate in cases of infection with the latter micro-organism was 21·3%; it was seldom isolated from the faeces or from healthy carriers. In most cases the cultures were derived from parenteral sources and from material obtained at necropsy. No deaths were due to *S. paratyphi A*, a type which is rarely found in the United States. Another rare type was *S. havana* which was originally isolated in 1939 from material from 21 newborn babies in a maternity hospital in Havana. The infection produced the signs and symptoms of acute meningitis and every baby died.

The mortality was about 2% in patients aged between 1 and 50 years, 5·8% in infants, and 15% in elderly patients. In about one-third of the fatal cases occurring in patients aged more than 50 years the infection was a terminal event in diseases such as hypertension, pneumonia, and cancer; as these patients had become debilitated it was possible for salmonellae to pass from the intestinal tract into the blood stream. Although acute gastro-enteritis was a common cause of death, especially in infants, the clinical manifestations of salmonella infection included meningitis, pneumonia and pleurisy, septicaemia, and bacterial endocarditis. Other manifestations were cholecystitis, appendicitis, peritonitis, and typhoid syndromes. *A. Garland*

2586. ***Haemophilus influenzae* Meningitis. Report of Five Cases**
J. SANDILANDS. *Lancet* [*Lancet*] **2**, 52–54, July 8, 1950. 12 refs.

Of the 6 cases of non-tuberculous meningitis admitted to a small hospital in Cornwall during a 2-year period 5 were due to *Haemophilus influenzae* and are reported in detail in this paper. Four cases occurred in children aged about one year, and one in a boy of 12; 2 of the 5 patients survived. There was some diagnostic difficulty in all cases, there being a pyrexial illness without definite signs pointing to the meninges in the early stages. Headache was an early symptom, but the appearance of definite meningism might be delayed for periods up to 2 weeks from the onset. Convulsions occurred in 2 cases. The diagnosis was made by lumbar puncture, a fluid with a high polymorphonuclear leucocyte count and swarming with Pfeiffer's bacilli being found. The author considers that in treatment streptomycin is the drug of choice, being administered intramuscularly; it is probably not necessary to inject it intrathecally.
F. B. Cockett

2587. ***Erysipelothrix rhusiopathiae*. Bacteriology and Chemotherapy**
M. WOODBINE. *Bacteriological Reviews* [*Bact. Rev.*] **14**, 161–178, June, 1950. Bibliography.

Erysipelothrix rhusiopathiae causes a disease in swine, sheep, birds, and fish. The infection is transmissible to man, causing an erysipeloid condition and occasionally septicaemia, meningitis, and endocarditis. Sulphonamides are useless but penicillin is of value in treating the disease in man and in birds, particularly turkeys. For reasons which are not apparent penicillin is valueless for treating the disease in pigs although the strains are quite susceptible to penicillin *in vitro*. In human beings the infection is usually seen in slaughterhouse men and in fish-handlers. *G. M. Findlay*

2588. **Failures with Aureomycin in the Treatment of Infection with *Brucella suis*. A Report of Three Cases**
T. W. GREEN and L. STEIN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 380–382, Sept. 30, 1950. 2 figs., 4 refs.

TUBERCULOSIS

2589. **Nursing and Tuberculosis in a General Hospital**
K. P. BALL, H. JOULES, C. H. C. TOUSSAINT, and J. A. HEADY. *Lancet* [*Lancet*] **2**, 121–125, July 22, 1950. 4 figs., 6 refs.

By adopting precautions designed to reduce the risk of tuberculous infection in hospital workers, the authors have shown that the incidence of such infection among nurses in a general hospital need be little greater than that

in comparable sections of the general population. Observations were made on 190 nurses on the staff of the Central Middlesex Hospital, who were followed up for several years. The Mantoux conversion rate was 27·9% for the first year, which is considerably lower than rates found for student nurses in the Prophit Tuberculosis Survey, and the low rate can justifiably be attributed to precautions used at this hospital. The annual morbidity from tuberculosis in these nurses was also low, being 8·7 per 1,000, a figure similar to that arrived at by the Prophit Survey for nurses in hospitals admitting few cases of tuberculosis, whereas the hospital concerned has 58 tuberculosis beds in two wards, the nursing staff of which is drawn from the staff of the hospital as a whole. When a diagnosis of open tuberculosis is made in a general ward, the patient is immediately transferred to one of the tuberculosis wards, one emergency bed in each being kept vacant for this purpose. Tuberculin-negative nurses are not allowed to work on the tuberculosis wards, the staff of which wear gowns while at work and, in addition, wear face-masks while bed-making. The floors of these wards are oiled, and sputum-mugs are never handled by the nurses. *M. Daniels*

2590. **A New Concentration Method for Koch's Bacillus in Sputum Specimens.** [In English]
G. WIHMAN. *Acta Tuberculosea Scandinavica* [*Acta tuberc. scand.*] **24**, 172–176, 1950. 1 fig., 15 refs.

A new method is described for the concentration of sputum for examination for the tubercle bacillus. The specimen of sputum is diluted with normal saline and liquefied by incubation for 12 to 24 hours. The precipitate is mixed with pancreatin and sterile ox-gall, incubated for an hour, diluted with saline, and centrifuged. Smears are made from the precipitate. The proportion of positive fields found in smears prepared by this method was 80% greater than in direct smears of the same sputum when the Ziehl–Neelsen stain was used.

J. R. Bignall

2591. **Value of Tuberculin-jelly Test**
W. P. DICK. *British Medical Journal* [*Brit. med. J.*] **2**, 141–143, July 15, 1950. 7 refs.

The value of the tuberculin-jelly test for tuberculin survey work is discussed. The techniques employed are outlined and the superiority of the flour-paper (the trade name for a fine type of abrasive paper) technique for preparation of the site of the test is statistically established in a large series.

Compared with the Mantoux test with 1 in 1,000 old tuberculin (O.T.), the flour-paper jelly test gave 72 to 92% positive reactions. A comparison between three tuberculin-jelly preparations, containing 2 mg. of purified protein derivative (P.P.D.) per g., 60% O.T., and 85% O.T. showed rather surprisingly that the O.T. preparations are superior to P.P.D. The higher lipoid content of O.T. is thought to be responsible for the fact that skin penetration by the O.T. jellies is probably better. The importance of avoiding too energetic use of the abrasive paper is stressed. *E. Nassau*

2592. **On Reversion.** [In English]
A. K. LARSEN. *Acta Tuberculosea Scandinavica* [*Acta tuberc. scand.*] **24**, 103–113, 1950. 10 refs.

Out of 1,344 tuberculin-positive individuals who were retested by the Mantoux method after 1 to 11 years, 24 (1·8%) were found to give a negative reaction to 1 mg. of purified tuberculin. The annual reversion rate was 0·28%. In those patients who had previously been positive to 0·1 mg. of tuberculin the annual reversion rate was 0·096%, but in those previously positive only to 1·0 mg. the rate was 2·2%. Where the reaction to 1·0 mg. had been greater than 10 mm. in diameter the annual reversion rate was 0·9%, whereas with a reaction of less than 10 mm. in diameter the rate was 8%. It is concluded that although reversion does occur, its frequency is much less than has been claimed by many earlier investigators.

J. R. Bignall

2593. **Failure of Chloromycetin in the Treatment of Tuberculosis**
D. T. CARR, A. G. KARLSON, and J. H. GAINER. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **25**, 316–319, June 7, 1950. 1 fig., 3 refs.

Chloramphenicol ("chloromycetin"), though only weakly tuberculostatic *in vitro*, was tested against experimental tuberculosis in guinea-pigs; no definite beneficial effect was obtained. Furthermore the drug did not affect the course of miliary tuberculosis in a human patient. The latter infection was caused by streptomycin-resistant tubercle bacilli, but chloramphenicol *in vitro* is equally bacteriostatic to streptomycin-sensitive and resistant organisms. It is concluded that chloramphenicol is of no value as an antituberculous agent.

P. D'Arcy Hart

2594. **Experimental Tuberculosis and its Chemotherapy**
B. CROSHAW and L. DICKINSON. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 178–187, June, 1950. 33 refs.

Of 1,000 compounds belonging to 11 chemical series (including aliphatic amidines, guanidine derivatives, and basic phenolic ethers), 24 showed tuberculostatic activity promising enough to warrant tests in infected guinea-pigs or mice, but none of these new drugs proved active. Certain combinations of drugs used as controls in these *in vivo* tests were more effective than either drug alone; these combinations were "sulphetrone" with streptomycin or licheniformin, and *p*-aminosalicylic acid with streptomycin. *p*-Aminosalicylic acid was more effective subcutaneously than orally in guinea-pigs.

P. D'Arcy Hart

2595. **The Chemotherapy of Experimental Tuberculosis in Mice**
A. R. MARTIN and G. T. STEWART. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **31**, 189–195, April, 1950. 3 figs., 10 refs.

Carefully planned and executed experiments were carried out on the use of murine tuberculosis in the evaluation of chemotherapeutic agents. Groups of mice, with from 20 to 50 animals in each, were infected

with 0·75 mg. of a virulent human strain of tubercle bacillus (" M.Tb. 905 ") to produce acute disease, or 0·02 mg. to produce a more chronic disease, and were treated with streptomycin (1,000 units per 20 g. mouse), *p*-aminosalicylic acid (1% in the food, approximately 40 mg. per mouse), and *p*-ethylsulphonylbenzaldehyde thiosemicarbazone (" No. 8388 ") (0·25% in the food, approximately 10 mg. per mouse per day). The smaller groups served for the collection of data on weight changes and mortality, the larger groups for obtaining histological information at various intervals. Three sets of experiments were carried out on comparable pairs of groups of mice. In one the drugs were administered continuously from the day of inoculation until death, and in the second for the first 14 days after inoculation. In the third experiment only streptomycin and 8388 were given, from the 21st day after infection until death. The efficacy of the drugs tested was in the order: streptomycin, 8388, *p*-aminosalicylic acid. The importance of making pathological studies at various stages of the infection is stressed. Delayed treatment (as in the third experiment) revealed the superiority of streptomycin even more clearly.

The findings suggest that retardation of the disease in experimental murine tuberculosis is the most that can be expected from the drugs tested. Therapeutic activity of the compounds was comparable in effect to reducing the numbers or the virulence of the bacilli inoculated. Murine tuberculosis provides a valuable means of screening, and to some extent of grading, chemotherapeutic agents. *E. Nassau*

2596. **Studies in the Chemotherapy of Tuberculosis; Part VI. The Comparison of Some Synthetic Substances with Streptomycin using Mice Infected with a Light Inoculum of *Mycobacterium tuberculosis***
E. HOGGARTH and A. R. MARTIN. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 188–194, June, 1950. 7 figs., 8 refs.

The authors varied their usual screening technique for possible antituberculous substances. Instead of a heavy inoculum (0·75 mg. moist weight) of *Mycobacterium tuberculosis* intravenously, which produces a necrotic tissue response, a lighter inoculum (0·02 mg.) was used; the lesions with the latter dose tended to be proliferative and the infection slower, though still progressive and unremitting. Some compounds found active previously were re-examined by the present method; apart from streptomycin they were given orally, usually from the time of infection onwards. The index of efficacy was survival time; in the controls deaths usually began in about 3 to 4 weeks and reached a 50% figure in about 1 to 3 months. In the tests, 4 : 4′-diaminodiphenyl sulphone [the parent substance of the various sulphones] and streptomycin were markedly active. The activity of a number of thiosemicarbazones was generally correlated with that shown after the heavier infection, the best of them giving better results than 4 : 4′-diaminodiphenyl sulphone or *p*-aminosalicylic acid, though worse ones than streptomycin.
P. D'Arcy Hart

2597. **Tracheo-bronchial Tuberculosis and Streptomycin.** [In English]
W. MASCHER and S. B. MATTSON. *Acta Tuberculosea Scandinavica* [*Acta tuberc. scand.*] **24**, 114–131, 1950. 2 figs., 19 refs.

The authors treated 22 patients with tuberculous tracheo-bronchitis with streptomycin. On bronchoscopy before starting treatment, granulations were seen in 20, ulceration in 7, and reddening and oedema only in 2. Stenosis, judged to be fibrotic, was present in 3 cases. Streptomycin was given by inhalation alone to 5 patients, 0·5 g. in 10 ml. of saline being administered by means of a nebulizer over four periods of 10 to 15 minutes daily. Nine patients received 1 g. daily intramuscularly, and 8 patients received streptomycin by both routes. Treatment continued for from 21 to 194 days. The bronchial lesion healed in 17 cases, improved in 3, and remained unchanged in 2. Of 15 patients who were bronchoscoped 2 to 9 months after the end of treatment, 3 showed relapse of the lesion. Five patients developed fibrotic stenosis during chemotherapy. Combined treatment with injection and inhalation is recommended. *J. R. Bignall*

2598. **Marital Tuberculosis Caused by a Streptomycin-resistant Tubercle Bacillus.** (Tuberculose conjugale de surinfection par bacille de Koch streptomycinorésistant)
J. BRUN, J. VIALLIER, J. C. KALB, and E. POMMATAU. *Lyon Médical* [*Lyon méd.*] **183**, 381–382, June 11, 1950. 1 ref.

A few cases of pulmonary tuberculosis due to streptomycin-resistant tubercle bacilli have been reported in nurses and hospital attendants. An instance is reported of a wife who was infected by her husband after he had received 100 g. of streptomycin. The strains isolated from both husband and wife grew well in the presence of 50 μg. of streptomycin per ml. although the wife had never received streptomycin. *G. M. Findlay*

2599. **Lessening the Risk of Streptomycin Resistance by Combined Sulphone–Streptomycin Treatment. A Study of 100 Cases of Pulmonary Tuberculosis.** (Abaissement du risque de streptomycino-résistance sous l'action d'un traitement conjugé streptomycine–sulfone. Etude sur 100 tuberculeux pulmonaires)
E. BERNARD, —. NOUVION, P. J. COLETSOS, and B. KREIS. *Bulletin de l'Académie Nationale de Médecine* [*Bull. acad. nat. Méd., Paris*] **114**, 461–466, July 4, 1950. 2 figs.

For this trial 100 adult male patients at Champrosay Sanatorium were selected. All had pulmonary tuberculosis, the duration of the disease ranging between 4 months and 5 years, with positive sputum and lung cavities, usually bilateral. None had had any previous chemotherapy. They were divided into two comparable groups of 50, the first group receiving streptomycin and sulphone, and the second streptomycin only. The sulphone was given thrice daily in a total daily dose of 90 mg. during the first week, 105 mg. during the second, 120 mg. during the third, 135 mg. during the fourth, and 150 mg. during the fifth and subsequent weeks. Streptomycin, 1 g. daily, was given by intramuscular injection for

132 days, commencing 7 weeks after the start of sulphone therapy. Various toxic reactions due to the sulphone were recorded.

The degree of resistance of the tubercle bacilli in the sputum of each patient was titrated every 15 days by the standard method of the Pasteur Institute. The results were as follows: after 42 days of streptomycin treatment the incidence of resistance was 38% in the first group, and 78% in the second group. After 70 days the figures were 51% and 91%, and after 122 days 48·5% and 90·6% respectively. These results were confirmed in another group of cases with long-standing cavities, in whom the development of resistance was likely to have been particularly rapid. The treatment, so far as the patients' clinical condition was concerned, was not considered to have been effective. *Donough O'Brien*

2600. **Aureomycin in the Treatment of Tuberculosis**
W. S. SCHWARTZ, S. T. WALTON, and R. E. MOYER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **61**, 875–880, June, 1950. 7 refs.

Three patients with pulmonary tuberculosis, 5 with tuberculous sinuses, and 2 with tuberculous laryngitis were given 3 g. of aureomycin daily by mouth for 30 days, in 250-mg. capsules 3-hourly from 6 a.m. to 9 p.m. All the cases were considered suitable for streptomycin therapy. Satisfactory blood levels of aureomycin were obtained on this dosage. Toxic effects were mild and transient though in one case the urine contained albumin and casts. The results indicated that this drug is of no value in the treatment of tuberculosis.
R. H. J. Fanthorpe

2601. **A Study of the Relation of Nutritional Status to Pulmonary Tuberculosis**
C. R. SHAW, F. BECK, H. PILCHER, and J. PARKER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 58–66, July, 1950. 1 fig., 24 refs.

The food intake and blood levels of haemoglobin, vitamin A, ascorbic acid, carotene, alkaline phosphatase, and total protein of 187 tuberculous patients in hospital were compared with those of 118 healthy persons. Food intake was found to be much the same in both groups, and the blood levels of the various substances were not significantly different in tuberculous and non-tuberculous subjects. The only definite finding was a low level of intake of all nutrients in tuberculous patients with severe symptoms (but not necessarily with a severe degree of disease). The authors do not offer any explanation for this finding. *John R. Forbes*

2602. **The Occurrence of Pulmonary Tuberculosis following Pulmonary Excision for Nontuberculous Diseases**
H. L. KATZ. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **61**, 835–844, June, 1950. 4 figs., 12 refs.

The need for a long-term follow-up of patients who have undergone pulmonary resection is illustrated by the 4 cases reported, in which the patients were found to have pulmonary tuberculosis within 5 to 16 months after pulmonary resection for non-tuberculous conditions, although there had been no evidence of tuberculosis before or immediately after the operation. In 3 cases in which only a portion of a lung had been removed the tuberculosis, which was already far advanced when diagnosed, had developed in the remaining part of the lung. *L. M. Franklin*

2603. **Pleural, Peritoneal, and Pericardial Tuberculosis. A Review of 209 Cases Uncomplicated by Treatment or Secondary Infection**
O. AUERBACH. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **61**, 845–861, June, 1950. 4 figs., 12 refs.

In a series of 2,333 necropsies on cases of tuberculosis carried out at Sea View Hospital, Staten Island, New York, tuberculosis of the serosal surfaces was found in 209 cases (8·9%). It was more commonly found in negroes than in whites. Tuberculosis of the peritoneum was found 131 times, of the pleura 103 times, and of the pericardium 28 times. In 49 cases more than one serosal surface was affected. In 114 cases the serosal lesions were associated with skeletal or urogenital tuberculosis. Tuberculous peritonitis was commoner in females than males, and was associated with tuberculosis of the Fallopian tubes in 60% of the former. Chronic pulmonary tuberculosis was present in only 25 of the 103 cases of pleural involvement. It is suggested that in most cases of pulmonary tuberculosis the pleural space has been obliterated by fibrous tissue before the pulmonary disease reaches the pleural surface of the lung, so that tuberculous pleuritis does not develop.
L. M. Franklin

2604. **A Study of 672 Cases of Artificial Pneumothorax.** (La colapsoterapia médica. Estudio de 672 neumotórax intrapleurales)
L. A. CABO REY. *Revista Española de Tuberculosis* [*Rev. esp. Tuberc.*] **19**, 457–484, July, 1950.

The clinical material for this work was drawn from the rural areas of Galicia, where active tuberculous infection is rife at present, as shown by the high percentage of primary infections after the age of twenty. The patients are mostly of the lower classes and arrive for treatment in the worst possible condition, most of them having advanced bilateral disease.

The author considers that pneumothorax should be induced in a sanatorium; only when the sputum is negative and the disease appears controlled should the case be transferred to a dispensary. The indications for pneumothorax are given as follows: (*a*) Primary infection with excavation. (*b*) Presence of an early focus of the Assmann type. These patients are watched and, if tubercle bacilli are found in the sputum or signs of excavation are discovered, a pneumothorax is established. (*c*) Early cavitation of any type. (*d*) Reactivation of old foci with dissemination, with or without excavation. (*e*) Tertiary cavitation, the cavity walls being hard and fibrosed. Thoracoplasty is carried out if the pneumothorax treatment shows little sign of success.

Cases were treated by the author partly in dispensary practice and partly in a sanatorium. In Galicia, there is one sanatorium of 125 beds for a population of 900,000, and a mortality rate of 1·66 per 1,000. Of 2,886

patients examined in the dispensary, 355 were accepted for pneumothorax, 72·7% being males. The results are given in the following table:

	Unilateral Pneumothorax		Bilateral Pneumothorax	
	Cases	Per cent	Cases	Per cent
Cured ..	128	40·5	9	23·1
Improved ..	42	13·3	11	28·2
No change ..	69	21·8	5	12·8
Worse ..	77	24·4	14	35·9

In the Sanatorium, out of 1,603 patients, 317 underwent pneumothorax treatment. The results were:

	Unilateral		Bilateral	
	Cases	Per cent	Cases	Per cent
Cured ..	95	36·6	15	26·3
Improved ..	36	13·85	19	33·4
No change ..	43	16·55	6	10·5
Worse ..	86	33·1	17	29·8

A study of these figures shows that the results of treatment in the dispensary (ambulatory) and in the sanatorium were practically the same. This may appear surprising, but the author notes that patients in poor general condition were admitted to the sanatorium. The complications are listed in the table below:

	Serous Effusion		Empyema		Spontaneous Pneumothorax	
	Disp.	San.	Disp.	San.	Disp.	San.
Unilateral pneumothorax	101	102	13	10	10	3
Percentage ..	31·9	39·2	4·1	3·8	3·1	1·1
Bilateral ..	7	12	2	1	1	1
Percentage ..	17·9	21·0	5·1	1·7	2·5	1·7

The following conclusions are drawn: (*a*) Out of 576 cases of unilateral pneumothorax, a cure was obtained in 38%. Out of 96 cases of bilateral pneumothorax, a cure was obtained in 25%. (*b*) After the age of 40 years, there was a considerable fall in the percentage of successes. Between the 10th and 40th years the results were comparable. (*c*) A complete pneumothorax was obtained in one-third of all cases The percentage of cure was higher in such cases (51·3%) than in the cases of incomplete pneumothorax (32·6%). It is noted that in nearly 50% of cases of complete pneumothorax, treatment failed, a proof that in the cure of tuberculosis factors other than mechanical ones are operative. (*d*) The chances of success were comparable in lesions of the upper, middle, and lower lung fields.

J. J. Giraldi

2605. **Apico-basal Diameters of the Lungs and Mediastinal Shift in Phrenic Nerve Crush and Pneumoperitoneum Therapy: A Study of Eighty Cases**
W. Fox. *Thorax* [*Thorax*] **5**, 183–193, June, 1950. 5 figs., 17 refs.

In 80 cases of pneumoperitoneum and phrenic crush the apico-basal diameters and mediastinal shifts were measured before and soon after treatment had started. Radiographs were taken with the patient erect and in full inspiration, the distance from tube to plate being 6 feet (1·8 metres). Patients with scoliosis, artificial pneumothorax, or thoracoplasty were excluded.

In left-sided paralysis the average ipsilateral rise of the diaphragm was 8·1 cm., and on the right side 2·6 cm. In right-sided paralysis the rise was 7·7 cm. on the same, and 2·4 cm. on the opposite, side. The average mediastinal shift was 1·5 cm. away from the paralysed side but, owing to the additional factor of cardiac rotation, the range of shift was greater in left-sided than in right-sided paralysis.

Mediastinal shift and reduction in apico-basal diameters occurred regardless of whether there was a free, thickened, or partially or completely obliterated pleura, nor was the former always confined to the lower part, for tracheal shift was seen also in 23 cases. There are three ways in which paralysis of the hemi-diaphragm can cause this shift, first, by increasing the intrapleural pressure on the paralysed side, secondly, by enabling the pneumoperitoneum to exert a pressure on the lateral side of the mediastinum, and, lastly, by depriving the lower end of the mediastinum of the diaphragmatic crus as an anchor. It is pointed out that, while the therapeutic effect is maximal on the paralysed side, the accompanying diminution in apico-basal and side-to-side diameters on the other side is of value in bilateral disease.

Donough O'Brien

2606. **A Modified Conception of Phrenic Nerve Crush and Pneumoperitoneum Therapy**
W. Fox. *Thorax* [*Thorax*] **5**, 194–199, June, 1950. 5 figs., 14 refs.

In 70 out of 80 cases of pneumoperitoneum and phrenic nerve crush, there was an average mediastinal displacement of 1·5 cm. away from the paralysed side.

The old idea that in these cases there is a reduction only in the apico-basal diameter must therefore be modified. There is in fact also a broadening of the lung field on the paralysed side, in part due to the mediastinal shift, and in part due to the increased upward and outward movement of both upper and lower ribs.

On the non-paralysed side there is a corresponding diminution in the side-to-side diameter, as well as a lesser degree of diaphragmatic rise. *Donough O'Brien*

2607. **A Study of the Mechanism of Healing of Tuberculous Processes of the Intestine under Chemotherapy.** [In English]
F. Boehm. *Acta Tuberculosea Scandinavica* [*Acta tuberc. scand.*] **24**, 30–37, 1950. 13 figs., 11 refs.

Intestinal resection was performed in 4 patients with pulmonary and intestinal tuberculosis after 11 to 15 weeks

of treatment with "TB I/698" (maximum dose 400 mg. daily). Examination of the specimens showed a considerable degree of healing of the tuberculous lesions. In all the specimens there were also lesions with clear signs of activity, and histologically the disease could not be said to be healed. In these severely ill patients, and also in others receiving the drug for minimal pulmonary disease only, liver biopsy showed extensive fatty infiltration, although the results of liver function tests were essentially normal and there was no clinical evidence of liver damage. *J. R. Bignall*

2608. **Second Part of Mass-examination for Tuberculosis in the Municipality of Copenhagen, 1947/48.** [In English]
M. HOLM, S. HOLM, and K. WINGE. *Acta Tuberculosea Scandinavica* [*Acta tuberc. scand.*] **24**, 182–200, 1950.

2609. **Collective Results of Mass-examinations for Tuberculosis in the Municipality of Copenhagen, 1946 and 1947/48.** [In English]
K. WINGE. *Acta Tuberculosea Scandinavica* [*Acta tuberc. scand.*] **24**, 201–221, 1950. 1 fig.

See also Section Pharmacology and Therapeutics, Abstract 2261; Section Pathology, Abstracts 2352–4; and *Abstracts of World Surgery*, 1950, **8**, 289.

PROTOZOAL INFECTIONS

2610. **The Liver in Malarial Subjects. (A Study of 45 Cases by Means of Puncture Biopsy).** (Le foie des paludéens. (Etudié sur 45 cas au moyen de ponctions-biopsies)
L. TELCHAROV and M. TODOROWA. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 2072–2075, June 10, 1950. 5 figs., 12 refs.

The authors state that the 45 patients studied had a tertian fever, and that the tissue changes seen in the three varieties of malaria are substantially similar in spite of the diverse clinical syndromes.

In the primary attack the liver mesenchyme varies considerably in appearance. Hyperaemia in portal areas is seen, together with perivascular lymphocytic infiltration in the portal region; these cells do not contain pigment or parasites. This infiltration has a tendency to lead to fibrosis; the process can be followed by successive biopsies. Cellular mobilization is represented by a tendency of the endothelial cells to revert to the monocytic form. Some phagocytosis may be seen, and there is an exudation of serous fluid, sometimes haemorrhagic, into the spaces of Disse and, to a lesser extent, the periportal spaces. The parenchyma shows a reduction in glycogen, a retention of biliary pigment with some dilatation of bile caniculi, and a slight retention of iron pigment. Neither malarial pigment nor parasites were observed within the parenchymal cells.

The picture in relapses is complicated by the occurrence of secondary infections. In the mesenchyme the mobilized elements become fixed, and in periportal areas there is an increase in fibrous tissue. Kupffer cells contain pigment and may ingest erythrocytes. In 3 cases nodules formed of mononuclear cells with fibrotic elements and giant cells were observed, the latter mostly being charged with malarial pigment: these nodules are compared to those occurring in Hodgkin's disease. They were present when secondary infection occurred, and the term paramalaria is used to describe this state. Perivascular cuffing with both lymphoid tissue and granulocytes was found. A marked tendency to sclerosis was present in chronic malaria, with the production of a pre-cirrhotic state. The parenchyma undergoes fatty degeneration, hypotrophy, and degeneration, especially at the centre of the lobule. The biliary vessels are distorted by fibrous tissue.

Early in the disease, parasites are found equally in liver smears and in peripheral blood. Later a preponderance is seen in the liver blood. The authors believe that this is due to immunity, and state that in early stages ingested parasites show less degeneration than the engulfing cell; later this picture is reversed, but intermediate stages occur.

The authors cannot confirm that the exoerythrocytic cycle takes place in parenchymal cells. They believe that after sporozoites have been ingested by an infected mosquito they are engulfed by hepatic histiocytes where they are able to develop. On one occasion only was a parasite (schizont) seen within a parenchymal cell in man.

[There are several anomalies in this paper, and the precise meaning is not always clear. The findings are at variance with those obtained by many authors on post-mortem material, and further work is obviously required.] *W. H. Horner Andrews*

2611. **An Experimental Study of the Effect of Adrenocorticotrophin in Chagas's Disease.** (Nota preliminar del estudio experimental sobre la accion de la hormona adrenocotrofica de la hipofisis en la enfermedad de Chagas)
J. ROBLES GIL and M. PERRÍN. *Archivos del Instituto de Cardiología de México* [*Arch. Inst. cardiol. Méx.*] **20**, 314–326, June 30, 1950. 8 figs., 3 refs.

2612. **Treatment of Amebiasis with Bacitracin**
H. MOST, J. W. MILLER, E. B. GROSSMAN, and N. J. CONAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 792–794, July 1, 1950. 3 refs.

Bacitracin was given by mouth to 51 patients with amoebiasis, 48 of whom were asymptomatic or had mild symptoms and 8 moderately or seriously ill. The total daily dose varied from 40,000 to 120,000 units and treatment was given for 5 to 10 days. The recommended dose is 80,000 units daily for 10 days.

In 34 cases (66%) the patient was apparently cured after a single course, but only one-third of those needing more than one course were cured. In all 8 severe cases clinical recovery was complete, the ulcers healed and the amoebae disappeared, but relapse occurred in 4 of them after periods ranging from 5 to 350 days. [It seems possible that reinfection may have occurred in some of these cases.] In one case bacitracin was effective after other amoebicides and antibiotics, including aureomycin, had failed to terminate the infection. Little bacitracin, if any, is absorbed from the

gut; in 5 patients none could be found in the blood or urine 2 or 4 hours after a single dose of 10,000 to 50,000 units. Toxicity was negligible. *A. W. H. Foxell*

2613. The Treatment of Amebiasis with Aureomycin
L. V. McVay, R. L. Laird, and D. H. Sprunt. *Southern Medical Journal* [*Sth. med. J.*] **43**, 308–313, April, 1950. 2 figs., 8 refs.

The multiplicity of so-called amoebicides suggests their inadequacy, a view borne out in practice. Aureomycin has proved to be active *in vitro*, so four daily oral doses of 500 mg. were given in 37 cases of amoebiasis, soon after meals in order to minimize gastric irritation. The follow-up period ranged from one to 6 months, and 7 to 24 stool examinations per patient were made by various methods, including culture. Of the 37 cases 29 were asymptomatic. Two patients had dysentery with hepatitis, and one had a liver abscess. Eight children and one pregnant patient were included, and there had been a mild febrile condition in the majority before treatment. The drug was found to be well tolerated, gave rapid relief in the severe cases, and was effective in 36 out of 37 cases in banishing cysts and vegetative forms from the stools. *Clement Chesterman*

2614. Aureomycin and Amoebic Dysentery
T. G. Armstrong, A. J. Wilmot, and R. Elsdon-Dew. *Lancet* [*Lancet*] **2**, 10–12, July 1, 1950. 8 refs.

The clinical trials described in this paper were carried out in Durban. Aureomycin was given to 52 African patients with acute amoebic dysentery, 5 African patients with attacks of exceptional severity, and 4 Europeans with a milder attack. The attack was the first in all but 6 of the 52 cases; blood, mucus, and vegetative *Entamoeba histolytica* were present in stools. Sigmoidoscopy was performed daily until colonic ulcers had healed.

Aureomycin was given by mouth in doses of 0·25 g. four times daily at 6-hour intervals for 15 days. The results are summarized in the following table:

Results of Treatment of 52 Cases of Amoebic Dysentery with Aureomycin

	Days of Treatment			
	10	15	20	27
Success	35	40	49	48
Possible failures ..	16	7	2	2
Absolute failures ..	1	1	1	1
No sigmoidoscopy	—	4	—	—
Totals	52	52	52	51

[Possible failure=usually symptom free. One or more ulcers still open but amoebae not found in stool or scraping.]

The rate of healing was remarkable and the mucous membrane between ulcers returned rapidly to normal. Diarrhoea usually ceased in 1 or 2 days, and the amoebae disappeared rapidly. Follow-up was difficult. One month after discharge 27 patients returned, 7 of whom had active colonic amoebiasis.

Of the 5 severe cases 2 ended in complete recovery; another recovered but stricture of the rectum developed subsequently. Emetine administration was added to the therapy before the 4th patient recovered. The 5th was a fulminating case and the patient died on the 2nd day of treatment. The 4 Europeans were all apparently cured.

The authors compare aureomycin therapy favourably with other forms of therapy tried under similar conditions. They suggest, however, that the antibiotic should be combined with another known amoebicidal agent.
W. H. Horner Andrews

2615. The Serological Diagnosis of Kala-azar. (Diagnostico serologico del kala-azar)
A. Fernández-Delgado de la Peña and M. D. Carmona. *Acta Pediatrica Española* [*Acta pediatr. esp.*] **8**, 699–704, June, 1950.

The authors report on the Gate–Papacosta complement-fixation test with an antigen prepared from a methylated alcoholic extract of *Myobacterium tuberculosis* which is not very specific for tuberculosis. In cases of infantile kala-azar it gave more positive results than did the serum-formalin reaction. Out of 14 cases of kala-azar only 2 gave a negative reaction, although with the formaldehyde test 9 were negative. In 11 control tests in cases of other diseases the complement-fixation test and the formalin reaction were only once positive. *Franz Heimann*

See also Section Pharmacology and Therapeutics, Abstracts 2262–4.

FUNGUS INFECTIONS

2616. Aspiration Biopsy of Bone Marrow as an Aid in Diagnosis of Histoplasmosis. Report of a Case
P. T. Pratt, S. O. Schwartz, and L. Ehrlich. *Archives of Internal Medicine* [*Arch. intern. Med.*] **85**, 893–899, June, 1950. 3 figs., 34 refs.

A case of histoplasmosis in a Russian Jewish man, aged 70, is reported. He had had a productive cough, worse at night, and anorexia for several months. On examination he was emaciated and dehydrated, and the skin was bronzed all over except in the "shoe" area. The chest was dull to percussion in the left upper zone and the right lower zone, where the breath sounds were increased. Scattered rales were heard all over the posterior surface of the chest, loudest over the right lower zone. The liver was enlarged to 3 cm. below the costal margin; the spleen was not palpable. Erythrocyte and leucocyte counts were low. A blood film showed normochromia, moderate anisocytosis, and poikilocytosis. Nine days after admission there was bilirubin and excess of urobilinogen in the urine, and serum gave a 3+ result in the cephalin-flocculation test, the thymol turbidity being 12·1 units and the icteric index 11 units. Radiographs showed a rounded opacity in the left upper zone of the chest and translucency of the right semilunar bone and head of the right first metacarpal bone.

Sternal puncture revealed a hypercellular marrow with an erythroid–myeloid ratio of 1 : 2. Occasional band cells of pernicious-anaemia type, rubricytes, and metarubricytes were also found There was a marked increase in the number of histiocytes and many contained from 1 to 20 organisms in their cytoplasm, the organisms being identified morphologically as *Histoplasma capsulatum*. Re-examination of blood films showed the occasional presence of the fungus in monocytes. The bone marrow was cultured in Littman's medium, and the tuberculate chlamydospores of *H. capsulatum* were grown. Blood culture in brain broth was positive. The patient was treated with penicillin, multiple vitamin preparations, and liver extract, but his temperature continued to swing between normal and 102° F. (38·9° C.) and he died 12 days after admission.

At necropsy a caseous grey area, 0·5 cm. in diameter, was seen in the upper lobe of the left lung. It was surrounded by several greyish, translucent nodules 1 mm. in diameter. Several similar nodules were found in the spleen, which was enlarged. The liver was slightly enlarged, with a few adhesions between it and the diaphragm. The bone marrow was red and hyperplastic. Histologically, the lesions in the lung consisted of large granulomata composed of plasma cells, fibroblasts, epithelioid cells, and histiocytes; Langhans giant cells were seen. The lesions were more vascular than fresh tubercles. The fungus was present in the histiocytes and giant cells. The general architecture of the spleen was intact, but some scattered histiocytes contained *H. capsulatum*. The portal fields in the liver were increased in size, with fibrous projections. In the centre of the lobules the hepatic cells were almost completely destroyed and replaced by histiocytes containing *H. capsulatum*. The fungus was occasionally seen in the macrophages of the pancreas, adrenals, and bone marrow. It stained red with Mallory's stain, dark blue with Goodpasture's stain, and light blue with Custer's stain. The authors advocate routine examination and culture of the bone marrow where this disease is suspected. In only 5 of the 113 reported cases was the fungus seen in blood films. *Walter H. H. Merivale*

2617. **The Clinical Picture associated with Infections due to *Cryptococcus neoformans* (*Torula histolytica*). Report of Three Cases with Some Experimental Studies**
A. M. FISHER. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **86**, 383–414, June, 1950. 6 figs., 34 refs.

Cryptococcosis (or torulosis) is a rare affection caused by *Cryptococcus neoformans*, a yeast-like organism. It may either cause localized abscesses or slowly spread by the lymph and blood streams to infect various tissues and organs, among them almost always the central nervous system. The author describes 3 cases admitted to the Johns Hopkins Hospital. In the first there were two localized lesions, one of them in bone, and local surgical treatment and iodine therapy, both local and internal, were successful. In the second and third cases the infection was general: in one it was associated with widespread sarcoidosis and spread throughout the body tissues and organs; in the other there was a meningoencephalitis and also a focus in one kidney. Both these cases terminated fatally and were apparently uninfluenced by any treatment.

The author reports animal experiments by which he investigated the virulence of the organism and its response to chemotherapy; it was resistant both to sulphonamides and antibiotics. *W. G. Harding*

2618. **Further Observations on Histoplasmosis. Mycology and Bacteriology**
M. L. FURCOLOW. *Public Health Reports* [*Publ. Hlth Rep., Wash.*] **65**, 965–994, Aug. 4, 1950. 20 figs., 10 refs.

HELMINTH INFECTIONS

2619. **Trivalent Sodium Antimony Gluconate in the Treatment of Schistosomiasis**
M. ERFAN and S. TALAAT. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **44**, 123–126, July, 1950. 2 refs.

A preliminary report is given on the treatment of schistosomiasis with tervalent sodium antimony gluconate. This compound is very soluble but somewhat unstable in solution and must not be dissolved in water until just before injection. The dose was 3 ml. of a 6% solution given intravenously on 6 (later 12) successive days for an adult weighing 60 kg., the total dose thus being 1·08 or 2·16 g. Thirty patients with urinary schistosomiasis were treated with a 6-day course, and 6 with a 12-day course. At examination 1 to 2 months later the urine of 17 of the 30 patients contained no ova, and of 5 others only dead ova; the remaining 8 patients passed living ova. Of the 6 patients treated with a 12-day course, 3 passed no ova, and 3 dead ova, in the urine 1 to 2 months later. Two patients vomited after the 4th and 5th injections and one developed an urticarial rash, which lasted only one day. The rest had no untoward reactions; there was no coughing such as occurs after the administration of tartar emetic.
F. Hawking

2620. **Larval Ascariasis as a Cause of Chronic Eosinophilia with Visceral Manifestations**
R. D. MERCER, H. Z. LUND, R. A. BLOOMFIELD, and F. E. CALDWELL. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 46–58, July, 1950. 5 figs., bibliography.

A syndrome recently described by several authors, characterized by chronic eosinophilia and eosinophilic granuloma of the liver, pyrexia, leucocytosis, hyperglobulinaemia, and pulmonary changes, is fully discussed in relation to a case of larval ascariasis in a child of 2 years. There was a long history of chronic ill-health with mild fever and marked irritability. The abdomen was distended; the liver and spleen were enlarged. The haemoglobin content of the blood was 6·2 g. per 100 ml., erythrocyte count 3,700,000 per c.mm., and the leucocyte count was 38,000 per c.mm., 62% of the cells being eosinophils. The serum protein content was 6·98 g. per 100 ml. and globulin was much in excess. Stools

were repeatedly negative for ova and parasites. *X*-ray examination of the chest showed infiltration in the upper lobe of the right lung, with increased hilar markings. A biopsy of the liver revealed *Ascaris* larvae and inflammatory foci of granulomatous and exudative types. Eosinophilia and plasma cells predominated in these foci. Eventually an adult male *A. lumbricoides*, 6 inches (15 cm.) long, was passed per rectum and three separate courses of hexylresorcinol were given, after which the stools remained free of ova and worms. This was not the end of the case, however, as the patient was readmitted 2 months later with return of symptoms, the pulmonary signs being particularly marked. Antihistamine therapy was prescribed and during the 14-day hospital course steady improvement occurred. The liver and spleen were seen to shrink and *x*-ray examination of the chest revealed clearing in all areas. An ascaris skin test was strongly positive. Allergy to the ascaris had undoubtedly played an important part in the production of the clinical picture. Further investigation revealed ova-infested dirt in the basement of the child's home, which she had frequently been seen to eat. This was no doubt the source of the repeated doses which resulted in her sensitized state. An interesting discussion follows of the resemblance of this case to tropical eosinophilia and chronic Löffler's syndrome.

Ronald S. McNeill

2621. **The Problem of Loiasis in West Africa with Special Reference to Recent Investigations at Kumba in the British Cameroons and at Sapele in Southern Nigeria**

R. M. GORDON, W. E. KERSHAW, W. CREWE, and H. OLDROYD. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **44**, 11–47, July, 1950. 10 figs., bibliography.

This is a general account of the problem of loiasis in West Africa, with particular reference to the work done by the authors at Kumba in the British Cameroons, where a research station was established in 1949, and at Sapele, in Southern Nigeria.

Apart from two doubtful exceptions, the disease is confined to the equatorial rain forest of Africa, which extends from latitude 8° N. to latitude 5° S., and from the Gulf of Guinea eastwards to the Great Lakes. The genus *Chrysops*, in which development of the microfilariae of *Loa loa* takes place, is represented in almost all parts of the world, but the subgenus *Kleineana*, which contains all the known and suspected vectors of *L. loa*, is limited to Africa. *C. silacea* and *C. dimidiata* are restricted to the rain forest region, and in this part there is little doubt that they are the only important vectors; at the fringes of the forest it is possible that other species (for example, *C. distinctipennis* in the Southern Sudan) may act as vectors. *C. longicornis* probably does not transmit the disease.

At Kumba, of 2,000 adult flies collected all were *C. silacea* or *C. dimidiata*, but when larvae were gathered and reared they produced also *C. longicornis*, *C. langi*, and *C. griseicollis*, none of which had been known to occur at Kumba. This suggested that they must live disassociated from man, presumably feeding on animals, among which monkeys might form a reservoir of filarial infection. The larvae of *Chrysops* are found in densely shaded streams where the course is impeded by vegetation, the flow is slow, and the bottom is covered by decaying leaves over soft mud over fine sand. The adult fly bites chiefly between 8.30 a.m. and 5.0 p.m., but it is averse to feeding in full sunlight. The adult females of *C. silacea* and *C. dimidiata* normally live in the forest canopy. Europeans at Kumba are bitten mostly in the shade of their houses, which stand on a high ridge at the level of the tops of the high trees growing in the adjacent valleys so that they form interruptions in the forest canopy; the flies seldom enter the African houses, which are lower in position. The female flies entering the houses probably hunt by sight and are attracted by moving objects. In the forest around Kumba visibility at ground level is severely restricted by vegetation; therefore *Chrysops* is not attracted down from the forest canopy and the impression is given that *Chrysops* is absent from such areas. When a platform was erected 50 feet (15m.) up a tree, or when a clearing was made in the undergrowth below, specimens of *C. silacea* were readily captured. On the rubber plantations at Sapele in Southern Nigeria the picture is quite different. Both species of *Chrysops* feed voraciously throughout the plantation area and enter the well-lighted European houses (while avoiding the dark African houses). This is because the rubber trees are low-growing and persons on the ground can easily be seen by flies in the canopy above. Male *Chrysops* do not feed on blood; none was captured during the investigation and their habitat is still unknown.

Among 22 adult Africans examined at Kumba at noon the density of microfilariae in the blood varied between 1 and 1,500 per 50 c.mm. *Chrysops* feeds from a pool of blood which collects when the tissue is lacerated by the proboscis, the average amount of blood taken by *C. silacea* in one meal being about 10 to 40 c.mm. The average infection rate among flies at Kumba is about 7·2%; although many worms are often present in an infected fly, they do not seem to have an adverse effect on it. When an infected fly feeds, large numbers of infective larvae emerge and are deposited on the surface of the skin, from which they disappear rapidly. The exact way in which the larvae penetrate the skin is, however, still obscure. The development of the adult worm in man probably takes between 6 and 18 months, but practically nothing is known of this phase of the life history. The fully adult worm may occur in almost all anatomical regions, but it is always confined to connective tissue. In man their rapid translatory movements have been observed only in the subcutaneous tissue and conjunctiva, but in monkeys similar worms have been seen moving along intermuscular septa and other fascial planes. Many patients with loiasis appear to have no microfilariae in their blood, but it is suggested that in a large proportion of these cases microfilariae can be detected by repeated examination and that in the remainder the microfilariae may accumulate in a reservoir in the internal organs.

Whereas the treatment of loiasis by chemotherapy has developed rapidly during the last 5 or 6 years, "hetrazan" appearing to be the most effective drug,

its effective control requires the accumulation of more information. Dimethyl phthalate (60%) is a satisfactory repellent of *Chrysops*. Extensive clearing of the forest would probably be effective (but would be expensive), but it is doubtful whether spraying with DDT would be effective in destroying the adult flies. Methods for control of the larvae will probably be feasible, but they still require more investigation.

[This is an interesting and detailed paper which contains more information than can be conveyed in an abstract. Various points were amplified in the subsequent discussion.] *F. Hawking*

2622. **Hetrazan in the Treatment of Filariasis due to *Wuchereria malayi***

T. WILSON. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **44**, 49–66, July, 1950. 6 figs., 11 refs.

The investigations reported took place at Sungei Patani in the north-west corner of the Malay peninsula, where an endemic area of filariasis due to *Wuchereria malayi* occurs. The patients were mostly symptomless carriers of microfilariae, who were persuaded with difficulty to enter hospital for treatment and who would accordingly take a serious view of any untoward reaction produced by the treatment. The first 3 patients had microfilariae in the blood but no symptoms, and received 1·7 to 2·15 mg. of " hetrazan " citrate (containing 51% base) per kg. body weight thrice daily for 21 days. They developed a severe reaction within 6 to 12 hours of the first dose, with pyrexia to 103° F. (39·4° C.), severe headache, nausea, and vomiting. The symptoms had abated considerably by the 3rd day and disappeared completely by the 5th. A 4th patient with symptoms of filariasis but no microfilariae had no reaction except a mild urticarial rash on the 6th and 7th days. The microfilarial count in the first 3 cases diminished dramatically; in 2 patients whose night blood contained 1,200 and 750 microfilariae per 60 c.mm. respectively, it was reduced to 6 per 60 c.mm. after three doses had been given in 9 hours. In the second group, consisting of 3 symptomless microfilaria carriers, the dose of hetrazan given was 1·1 to 1·6 mg. per kg. thrice daily. The febrile reactions were similar, but a little less intense and prolonged; the effect on the microfilariae was the same.

Including the cases described above, hetrazan was given in all to 20 patients who had microfilariae in the blood but no symptoms of filariasis. The initial doses ranged from 0·28 to 2·15 mg. per kg. thrice daily. All had fairly severe reactions as described above, although the reactions were a little milder if the dose was below 1·0 mg. Once the reaction had subsided, the dose could be quadrupled without ill effect. The microfilarial count fell rapidly and in 15 out of 16 patients none was found at the end of treatment. In 2 patients 0·12 mg. per kg. was given thrice daily; this dose produced no reaction, but had no effect on the microfilariae. When the dose was raised to 0·25 mg. per kg. the microfilarial count fell slowly and a mild reaction took place. Eight patients with clinical filariasis but no microfilariae in the blood were given initial doses of 1·5 to 2·3 mg. of hetrazan per kg. without provoking any febrile reaction (except for one boy who, on the fifth day of treatment, had an attack of filarial fever with pain and swelling of one groin and leg). There was no significant improvement in the symptoms of filariasis. One man, who had both clinical symptoms and microfilariae in the blood, was given 108 mg. per kg. in 15 days; the microfilariae disappeared from his blood and the swelling of his leg disappeared. About 12 months later, 6 out of 11 microfilaria carriers were still free from microfilariae, while in the others the count was much reduced. Four of the patients with clinical symptoms, who were re-examined 10 months later, reported improvement in physical condition and in ability to work uninterrupted by filarial fever.

The reactions produced by hetrazan in the patients in this series were much more severe than those described by other authors as occurring in patients infected with *W. bancrofti*; this is possibly due to the different species of worm involved. *F. Hawking*

See also Section Pharmacology and Therapeutics, Abstracts 2265–6.

ACUTE RHEUMATISM

2623. **Preliminary Report on the Use of Sodium Gentisate in Acute Rheumatism.** (Prime ricerche cliniche sull'impiego del gentisato sodico nel reumatismo articolare acuto)

G. CAPRETTI and U. ARDUINI. *Giornale di Clinica Medica* [*G. Clin. med.*] **31**, 677–692, June, 1950. 8 refs.

Sodium gentisate was given by mouth in doses of 10 to 16 g. daily to 6 patients suffering from acute rheumatism. Results were disappointing, for in only 2 patients was there a complete remission. No evidence of gastric intolerance was seen, but drug rashes and alkaptonuria occurred. There is no point in substituting sodium gentisate for sodium salicylate in the treatment of acute rheumatism. *S. S. B. Gilder*

2624. **Treatment of Acute Rheumatism with Rutin and Ascorbic Acid.** (Tratamiento de la enfermedad reumática con rutina y acido ascórbico)

M. SCHNIR. *Semana Médica* [*Sem. Méd.*] **57**, 1143–1149, June 29, 1950. 29 refs.

The author treated 15 patients suffering from acute rheumatism in the Cosme Argerich Hospital, Argentina, with rutin and ascorbic acid. Patients were given 300 to 1,000 mg. of rutin daily, and 500 to 1,000 mg. of ascorbic acid. Total doses of rutin were 5 to 60 g., and of ascorbic acid 8 to 50 g. No untoward reactions were observed. All patients were cured, the criteria being disappearance of fever and of all articular, visceral, and cutaneous symptoms, return of the erythrocyte sedimentation rate to normal, and disappearance of all cardiac disturbances as measured clinically, radiologically, and electrocardiographically. Fever persisted for from 1 to 8 days, and articular symptoms disappeared between the 3rd and 21st days. The heart condition

became stabilized or returned to normal between the 10th and 35th days. The probable mode of action of the drugs is discussed, with special reference to changes in capillary permeability and fragility. *René Méndez*

2625. **Urinary Excretion of Glucuronic and Salicylic Acids in Normal and in Rheumatic Children**
J. C. S. Tseng, H. W. Elghammer, and A. C. Ivy. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **79**, 826–837, May, 1950. 1 fig., 24 refs.

Since glucuronic acid is a component of collagenous connective tissues, it was thought likely that a disturbance of glucuronic-acid excretion might be demonstrable in rheumatic subjects, and might provide a useful aid to diagnosis in rheumatic fever. However, the output of glucuronic acid in the urine was not specifically increased in children with rheumatic fever, except when acetylsalicylic acid was given. Administration of bicarbonate with acetylsalicylic acid lowered the plasma level of salicylic acid by increasing the excretion of the latter in the urine, at the same time decreasing the excretion of glucuronic acid. No therapeutic implications could be drawn from these observations. Ascorbic acid had no significant effect on glucuronic-acid excretion, and glucuronic-acid metabolism appeared to be similar in subjects with active and inactive rheumatic fever.
M. Baber

2626(*a*). **Certain Aspects of the Pharmacology of 3-Hydroxy-2-phenylcinchoninic Acid**
E. K. Marshall and E. H. Dearborn. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **87**, 36–49, July, 1950. 5 figs., 7 refs.

In deproteinized blood or urine, 3-hydroxy-2-phenylcinchoninic acid is determined by electrical fluorometry, metaphosphoric acid being used to remove proteins, and the centrifuged liquid being used for estimations. The drug is removed by *iso*propyl acetate, leaving fluorescent degradation products, similarly estimated. After addition of the drug to normal plasma, 98% could be recovered on estimation. In man, conjugation of the drug occurs to some extent and the compound is not removed by *iso*propyl acetate. After hydrolysis with hydrochloric acid the drug is freed and can then be extracted and estimated as before. These remarks also apply to the monkey but not to the rabbit or dog.

The drug is readily absorbed from the intestine in man and in the dog. In both a considerable amount is still present in the plasma after 24 hours. Comparatively little is excreted unchanged in the urine: 3% in man, 1% in the rabbit, but 6 to 14% in the dog. Only low values for the drug are obtained in the plasma of the rabbit, but it is thought that this results from rapid degradation rather than from failure of absorption. In the blood the drug is very largely bound to the plasma proteins.

Little evidence was obtained of either acute or chronic toxicity. In doses as high as 75 or 100 mg. per kg. intravenously it produces only transient symptoms in the dog. One dog did die from renal failure after a single oral dose of 100 mg. per kg., but others have received the same dose repeatedly with no signs of kidney damage. This amount given daily for 30 days caused some loss of weight, with anorexia and lethargy, possibly due to the production of gastric ulcer. Up to 400 mg. per kg. of the drug, given daily for 10 days to young rats, caused no signs of toxic effects. It was given daily for 30 days to 2 monkeys by mouth in a dose of 50 mg. per kg., and no ill effects resulted.
Reginald St. A. Heathcote

2626(*b*). **The Effect of 3-Hydroxy-2-phenylcinchoninic Acid upon Rheumatic Fever**
K. C. Blanchard, A. M. Harvey, J. E. Howard, A. Kattus, E. K. Marshall, E. V. Newman, and C. G. Zubrod. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **87**, 50–60, July, 1950. 7 refs.

Because of certain of its pharmacological actions, it was thought that this drug might be effective in diseases which respond to adrenocorticotrophin. As a preliminary trial, it was employed in acute rheumatic fever, in rheumatoid arthritis, in bronchial asthma, and in disseminated lupus erythematosus.

In 10 cases of rheumatic fever [with no control cases] it was given in a dose of 20 mg. per kg. on the first day, and thereafter for up to 20 days in a dosage of 10 to 20 mg. per kg. daily or on alternate days. The fever in almost all cases subsided within 2 days, but in 2 cases a low degree of fever persisted for some time. Joint pain and tenderness subsided almost equally rapidly, but swelling in a few cases persisted for some days. Three cases relapsed, 2 on the second and one on the fifth day. A second course produced a prompt response in 2 of these and there has been no further relapse in 3 months. The third patient became severely ill and died in spite of massive doses of aspirin. No change was observed in 3 other cases with myocarditis but no arthritis or fever.

Of 10 cases of rheumatoid arthritis, 2 showed objective, and the others subjective, improvement. One of the first 2 relapsed after 3 months and re-treatment then failed. In none were the results as dramatic as in the cases of rheumatic fever. The dose employed was 20 to 40 mg. per kg. for about 6 days.

No effect was obtained in 2 cases of bronchial asthma with 20 mg. per kg. for 7 days. In a third case double this amount produced moderate subjective improvement, possibly psychogenic, with no change in the chest signs. Two patients with disseminated lupus erythematosus were given 20 mg. per kg. In one case the condition improved somewhat for 10 days, but fever and arthritis then appeared, due to drug sensitivity. In the second case, in which arthritis and pleurisy were present, there was some improvement, though the arthritis did not disappear during 7 days' treatment. The condition relapsed soon after therapy ceased.

The drug seemed non-toxic, for in 80 patients (apart from one case of drug fever) the only side-effect noticed was irritation of the gastro-intestinal tract. When the drug was taken after meals and with an equal amount of sodium bicarbonate this was no longer seen. Even with a dose of 40 mg. per kg. daily for 10 days the only ill effect was that one patient complained of feeling light-headed. *Reginald St. A. Heathcote*

History of Medicine

2627. **An Early Attempt at Medical Reform in England, 1844–1845**

A. B. ERICKSON. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **5**, 144–155, Spring, 1950. Bibliography.

Among the early efforts to promote health legislation in Britain was the unsuccessful attempt in 1844 by the Home Secretary, Sir James Graham, to introduce a Medical Reform Bill, an episode which has been strangely neglected by medical historians. There was at that time great need for medical reform. Hygiene and sanitation had been totally neglected by the State, arrangements for sewage disposal hardly existed, the water was impure and the supply inadequate, and houses were dark, overcrowded, and insanitary. Many diseases were rampant under such conditions. There was no general control of medical practice, despite the efforts of the Royal Colleges and other bodies to secure a satisfactory standard, and quackery was widespread. Graham pointed out that each medical school had its own requirements and that some were even selling degrees. He advocated a " uniform and centralized system " governing education and licence to practise in medicine and surgery, and his scheme was to include a register of all who were fit to practise. Macaulay assured Graham of the support of the University of Edinburgh and of the Colleges of Physicians and Surgeons, but Wakeley denounced the Bill and stated that the general practitioners, who were outside the control of the aforementioned corporations, would strongly oppose it. Both predictions proved to be correct. The practitioners called the new measure a " Quack Protection Bill ", as it repealed the Apothecaries Act of 1815 and opened practice to unqualified persons. In the *Lancet* it was stated that the physicians would rank highest, next would come the surgeons, and in the lowest grade there would appear the general practitioners as the " degraded caste ". Some objected to the tyranny of control, others pointed out that no regulation had been applied to midwifery. The main opposition, however, was directed against the proposed Council of Health. Under such control, said the *Lancet*, " the independence of the profession is gone for ever, the Home Secretary becoming virtually a dictator, with the doctors in his power ". In almost every English town appeared a Medical Protective Society, with the defeat of the Bill as its object.

Nevertheless the Medical Reform Bill was not without its supporters. The *Edinburgh Medical and Surgical Journal* approved the Bill " to remove and rectify the abuses and evils " of medical practice. Admittedly it could not put an end to quackery, but the sick would always continue to employ any means they wished, and not always the regular practitioner. All that could be done was to prohibit the sale of patent medicines.

It was argued by the promoters of the Bill that the Government, in assuming control, had no desire to harm the profession, and that the idea of practitioners governing themselves was " completely Utopian ". As the result of lengthy discussion, Graham resolved to alter his Bill, and he presented it in a modified form in 1845. The Universities of Oxford and Cambridge were to be exempted, the Apothecaries Company was empowered to prosecute unregistered practitioners, and it was to be a penal offence for any one falsely to assume the title of physician, surgeon, apothecary, or doctor.

Even in its new form the Bill offended the bulk of the profession. It was said that registration would create an undesirable aristocracy among medical practitioners and that the independence of the profession would be destroyed. Furthermore, the scheme would not abolish quackery. Richard Quain, however, strongly defended the registration system and the *Edinburgh Review* was loud in its praises of the Bill. But the opposing parties were never reconciled, and Graham, disgusted and discouraged at finding his efforts to be so futile, gave up the struggle and withdrew the Bill. The time was not ripe for so drastic a reform. Nevertheless the discussions had stimulated an interest in public health which bore fruit in the Public Health Act of 1848, and Graham's Bill was the model used by those who, in framing the Medical Act of 1858, provided for a medical council, and for a system of registration similar to that which Graham had envisaged. Thus, the Medical Reform Bill, unsuccessful though it was, formed an important link in the chain of progress which culminated in the charter for Social Security in 1948.

Douglas Guthrie

2628. **An Antimalarial Drug Favoured in Italy for Half a Century.** (L'antimalarico che ha appassionato gli italiani per mezzo secolo)

V. BIANCHI. *Rivista di Storia delle Scienze Mediche e Naturali* [*Riv. Stor. Sci. med. nat.*] **42**, 73–81, Jan.–June, 1950. 2 figs., 40 refs.

In the first half of the nineteenth century malaria was still a scourge in Italy, particularly in Lombardy and Piedmont. Although quinine was isolated by Pelletier and Caventou in 1820, it was too costly for the poor who needed it most. Italian chemists therefore sought a cheaper substitute. Carlo Pavesi and G. Polli experimented with *Eucaliptus globulus*, *Laurus nobilis*, and *Iris florentina*, but the native drug which seemed to give the best results was the common box, *Buxus sempervirens*, and the first to make a systematic study of this was the Milanese pharmacist Baldassare Pavia, whose two sons Ambrogio and Felice were in turn proprietors and editors of the *Bollettino Farmaceutico*.

In 1830 Fauré had extracted a substance from the box which he called " buxine " or " boxine ". In 1848 Pavia began its large-scale extraction and succeeded in isolating another substance which he called " parabuxine ". After prolonged clinical trials in the hospitals of northern

Italy by Vitali, Melagnano and others, all with the most favourable results, it was found to have a marked anti-fermentative, antipyretic, and antimalarial action.

Between 1848 and 1869 it was the subject of numerous reports and papers describing the work carried on in the laboratories of the Italian universities. The great difficulty had been to obtain the alkaloid in its pure crystalline state; Pavia had succeeded in this, but Barbaglia condemned Fauré's so-called " buxine " as an impure compound.

In a series of papers Barbaglia reported his own comprehensive investigations of its properties and gave a critical review of all preceding researches. He determined the dosage (120 to 150 mg. in the form of powder or pill) which produced a marked effect rapidly and safely, and stated that it merited a primary place as a powerful febrifuge (*Boll. farm.*, 1870–1, p. 209). He described his own experiments and tests and said that one drop of sulphate of " buxine " on a glass slide had had a remarkable inhibitory and even lethal effect on a variety of micro-organisms.

Buxine was manufactured by Pavia at only half the cost of quinine and it might have been thought that the drug was assured of widespread use and a secure financial future, especially as Flückiger in 1870 gave it publicity by identifying it with" biberine " (discovered in 1834 by Rodie of Demerara in *Nectandra rodiei*), " pelosine " (discovered in 1838 by Wiggers in *Cissampelos pareira*), and " paricine " (discovered by Winckler in 1845 in *Cinchona para fusca* [*sic*, actually *Buena hexandra* Pohl]). But the work of Barbaglia, and of his successor P. E. Allessandri, was destined to remain buried in the contemporary journals. Foreigners who mention *Buxus sempervirens* at the most refer to Barbaglia. A recent attempt (1916) to use buxine as a substitute for quinine only threw a momentary light into the obscurity which hides both the drug itself and the work of the Italian scientists.

[The bibliography is a chronological list of the most important papers on the subject between 1830 and 1919.]

F. N. L. Poynter

2629. **Florentine Doctors at the Battle of Montaperti (1260).** (I medici fiorentini alla battaglia di Montaperti (4 settembre 1260))

I. CAPPELLINI. *Rivista di Storia delle Scienze Mediche e Naturali* [*Riv. Stor. Sci. med. nat.*] **42**, 15–50, Jan.–June, 1950. 3 figs., 18 refs.

2630. **An Unpublished Fourteenth Century Pharmaceutical Herbarium.** (Un inedito erbario farmaceutico del trecento)

T. GASPARRINI LEPORACE. *Rivista di Storia delle Scienze Mediche e Naturali* [*Riv. Stor. Sci. med. nat.*] **42**, 51–72, Jan.–June, 1950. 7 figs., 20 refs.

2631. **Müntahab: a Medical Book in Turkish Written for Celebi Sultan Mehmet in 1420.** (Abdülvâhab'in Çelebi Sultan Mehmed'e müntahabi)

A. S. ÜNVER. *Istanbul Universitesi Tib Fakültesi Mecmuasi* [*Istanbul. Univ. tib Fak. Mec.*] **13**, 105–114, 1950. 3 figs.

2632. **René Descartes (1596–1650). Philosopher, Mathematician, Physiologist**

G. JEFFERSON. *London Hospital Gazette* [*Lond. Hosp. Gaz.*] **53**, 69–73, June, 1950. 1 fig., 9 refs.

The author, whose charming exposition of the Cartesian philosophy is already well known, returns to the theme in this account of the life and works of René Descartes as viewed in the light of present-day knowledge. A recluse and a wanderer, Descartes left his native Touraine at the age of 32 and settled in Holland, where his cottage on the sand dunes is no longer recognizable. His years of military service brought him into touch with many persons and enabled him to read deeply in what he was pleased to call his " book of the world ", notwithstanding the fact that social life was insufferably boring to him. Determined to approach old problems from a new angle, he sought in mathematics a clue to the perennial riddle. If only accurate measurement could be applied to the physical world, he argued, all would become plain. The *Discours*, published in 1628, remains his best-known work and is, indeed, one of the world's prose masterpieces, a remarkable intellectual autobiography. His first axiom, " I think, therefore I am ", has become a hackneyed quotation. Descartes believed that from this foundation, with the aid of two certainties, namely, mathematics and God, he could construct for himself and for humanity at large a new and satisfactory philosophy. In his view, the reality of self was firm and sure. All knowledge must be learned; none was innate, none congenital.

From this fundamental beginning, Descartes proceeded to formulate a theory of reflex action, although, naturally, he was hampered by the lack of anatomical knowledge at that time. Small wonder that he was obliged to assign to the pineal gland at the base of the brain the function of presiding over both body and soul and thus preserving that balance of " dualism " which was the essence of his creed. Animals, he argued, were devoid of souls: they were mere automatons. Although we may smile to-day at the crudity of some of his notions, we cannot but admit that Descartes had made a brave attempt to explain the difficult physiology of the central nervous system. He was, in fact, the first real projector of the determinist school, and his writings, so full of theory, none the less deserve the close attention of all scientists who pursue the same line of research at the present day. Despite the marvellous advances in modern technology, the problem to which Descartes addressed himself still remains a mystery.

Douglas Guthrie

2633. **Dr. Robert James Graves (1796–1853)—a Biography**

D. A. CLARK. *University of Western Ontario Medical Journal* [*Univ. west. Ont. med. J.*] **20**, 69–75, June, 1950. 11 refs.

2634. **Dr. George Owen Willis, a Pioneer Queensland Surgeon**

E. A. COOK. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 795–799, June 17, 1950.

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PRINTED IN GREAT BRITAIN BY WILLIAM CLOWES AND SONS, LIMITED, LONDON AND BECCLES

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ABSTRACTS OF WORLD MEDICINE

A Monthly Critical Survey
of Periodicals in
Medicine and its Allied Sciences

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

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ABSTRACTS OF WORLD MEDICINE

UNDER THE DIRECTION OF

HUGH CLEGG, M.A., M.B., F.R.C.P., Editor, *BRITISH MEDICAL JOURNAL*

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